IMPERIAL MYCOLOGICAL INSTITUTE 6 JUN 1947

TROPICAL DISEASES BULLETIN

VOL. 44.] 1947. [No. 4.

MAIN CONTENTS :

	PAGES
Summary of Recent Abstracts. III. Malaria (*concluded*)	377–390
Malaria	390–403
Trypanosomiasis	403–406
Leishmaniasis	406
Fevers of the Typhus Group	407–414
Yellow Fever	414–417
Plague	417–421
Cholera	421–424
Amoebiasis and Intestinal Protozoal Infections	424–425
Relapsing Fever and other Spirochaetoses	426–429
Leprosy	430–432
Helminthiasis	432–450
Deficiency Diseases	450–452
Sprue	452–457
Haematology	457
Venoms and Antivenenes	458
Dermatology and Fungus Diseases	458–460
Heat Stroke and Allied Conditions	461–462
Miscellaneous Diseases	462–463
General Protozoology	464
General Entomology	464–469
Laboratory Procedures	470
Reports, Surveys and Miscellaneous Papers	470–472
Book Reviews	472–478

For detailed Contents see pp. ii, iv, vi, viii and x.

Issued under
the Direction of the
Honorary Managing Committee of the
BUREAU OF HYGIENE AND TROPICAL DISEASES,
Keppel Street, London, W.C.1.
(Telephone: MUSEUM 3041)

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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 44.] 1947. [No. 4.

SUMMARY OF RECENT ABSTRACTS.*

III. MALARIA.

(*Continued from p.* 274).

Treatment.

General.—NAPIER (p. 10) contributed to the *New England Journal of Medicine* a paper discussing the value of some old and some more recent antimalaria drugs. Though it is a short paper, the summary is interesting and informative. CHOPRA, R. N. and CHOPRA, I. C. (p. 304) show how failure of response to oral administration of antimalaria drugs may be due to delayed absorption resulting from inflammatory conditions of the intestinal mucosa and from hypo-acidity such as occurs in chronic dysentery and other infections.

BRATTON (p. 408) has used mice for testing the toxicity of antimalaria drugs, the drug being mixed with their food, and by this method he found that mepacrine hydrochloride was four times as toxic, and pamaquin hydriodide fourteen times as toxic, as quinine hydrochloride.

According to STEVENSON (p. 407) the distressing chill preceding the fever of the malaria attack can be relieved promptly, if calcium gluconate, 10 cc. of a 10 per cent. solution, is slowly injected intravenously, as soon as possible after the onset of the chill. In some cases the relief, says Stevenson, is almost instantaneous. The results were equally good in *P. vivax*, *P. falciparum* and mixed infections. Certain precautions are recommended: Care to see that the injection is intravenous; if the subcutaneous tissue is involved, necrosis may ensue. The procedure is contraindicated in cases of arrhythmia and bradycardia and in those receiving digitalis therapy.

Claims for reduction of an enlarged spleen and for amelioration of the associated symptoms have been advanced by PODLESKER (p. 13). He injected slowly, intravenously, 10 cc. of a 10 per cent. calcium chloride solution on each of five successive days. Contraction of the spleen throws the malaria parasites into the blood-stream where they are attacked by antimalaria drugs.

PLÖTNER (p. 393) finds that artificial fever *may* cause disappearance of malaria parasites [on the other hand, it may have no such effect] and is, therefore, worth trial in relapsing cases, in conjunction with chemotherapy. ZELIGS (p. 202) speaks of post-malaria headache which is quite refractory to

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1946, v. 43. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

the usual "headache remedies." It is in most cases frontal and is present in the early morning, improving as the day advances. Some patients find benefit from the oral administration of 100 mgm. of nicotinic acid.

Quinine.—MARSHALL and ROGERS (p. 98) have devised a colorimetric method for determining and estimating cinchona alkaloids, based on the formation of a coloured compound with bromothymol blue.

HALAWANI and NOR-EL-DIN (p. 1109) report a case of Raynaud's syndrome, leading to gangrene and loss of the toes of one foot, after intragluteal injection of quinine. The patient suffered from syphilis as well as from chronic malaria. GALUSHKINA (p. 300) made trial of irradiated quinine in the treatment of malaria. The febrile attacks were observed to cease rapidly, and no relapses were seen in patients kept under observation for 18 months.

HANZLIK and CUTTING (p. 820) conclude that a combination of quinine and epinephrine intravenously is a safe initial treatment in cases of cerebral malaria. They recommend 0·5 gm. quinine hydrochloride (or dihydrochloride) and 1 mgm. epinephrine, in 250 cc. of isotonic NaCl solution, injected over a period of not less than 30 minutes. Two, even three, such injections may be given in 24 hours.

When stocks of quinine were low in the war, FLOCH (p. 820) found that the use of adjuvants (resorcin and methylene blue) in a mixture with quinine for intramuscular injection, effected great saving in quinine.

Mepacrine (atebrin).—LANGE and MATZNER (p. 1109) describe methods, based on measurements of fluorescence, for detecting the distribution of mepacrine in the blood, skin and cutaneous appendages (the nails); the last was a good and ready indication whether the drug was being taken regularly. GINSBERG and SHALLENBERGER (p. 1007) noted that for 3–6 months after cessation of treatment with mepacrine, the Wood light reveals a fluorescence in the finger-nails; excretion is, therefore, delayed longer than was generally thought. KIERLAND and his co-workers (p. 1008) noted the same thing in persons who had been taking mepacrine for 5 to 21 months; the fluorescence began to fade three months after the drug was stopped and disappeared in 6–7 months. LIPPARD and KAUER (p. 526) observed, in men who had been taking mepacrine for 7–29 months, a slate-grey pigmentation of the hard palate starting near the midline and extending to the alveolar margin, and, under the nails, spreading from the centre of the nail-body, and of the skin adjacent to the nails of the toes. The pigment contains iron and may be haemosiderin.

MOST and HAYMAN (p. 1005) compared the relative efficiency of mepacrine and quinine in the treatment of acute attacks of *vivax* malaria. In each case treatment was started on the day after the onset of the attack. The mepacrine was given thus: 1 gm. in three divided doses on the first day, then 0·1 gm. thrice daily for six days, a total of 2·8 gm. Those on quinine were given 1 gm. three times on the first day, at 8-hour intervals and 2 gm. in three divided doses on each of the next 13 days, that is 29 gm. in the 14 days. In 48 hours mepacrine had cleared the peripheral blood of parasites in 77 per cent., but of those receiving quinine this result was observed in 44 per cent. only; moreover, the former proved to be more prompt in the control of symptoms. Patients with eczematoid or exfoliative dermatitis should not be given mepacrine, if they have had the drug before. TOOMEY (p. 1006) showed that mepacrine was better than quinine also in *falciparum* infections when tried on 883 European patients in Freetown, Sierra Leone.

ABBEY and LAWRENCE (p. 627) have dispelled the idea that the continued use of atebrin, in doses of one tablet (0·1 gm.) daily, affects the visual acuity of air-pilots. MAEGRAITH *et al.* (p. 99) gave mepacrine in doses of 0·4–0·7 gm. weekly for several months to healthy young adults and found that such doses, even continued for long periods, had no harmful effects on the blood.

SMITH and STOECKLE (p. 1109), from experiments with isolated heart-lung preparations of dogs, stress the danger of intravenous injections of mepacrine if it is given rapidly.

THOMPSON (p. 98) trying varying dosage of mepacrine on American soldiers who, in England, relapsed with benign tertian malaria contracted in the Mediterranean, observed that relapses were fewer when large initial doses, 0·6 gm. were given. To a few as much as 1·0 gm., was given as an initial dose, but they showed toxic symptoms—nausea, vomiting and diarrhoea, and in one patient, mental symptoms. The effect on the parasites was noted; the plasmodial pigment was clumped in 45 minutes and disintegration was complete in about 6 hours.

Mode of administration seems to play a part; YUDKIN (p. 406) notes a case in which the drug failed when taken orally, but brought about rapid cure when injected intramuscularly.

Cerebral disturbances following the taking of mepacrine have been spoken of by several authors. SHIERS (p. 706) recorded a case of marked cerebral excitement after taking mepacrine, even in small doses. MERGENER (p. 405) reports psychosis after 2·8 gm. of mepacrine taken in 5 days. VOLLMER and LIEBIG (p. 201) state that, although rarely, atebrin may give rise to acute central nervous symptoms, and they mention illustrative cases, one in which a severe maniacal attack came on suddenly and lasted for nearly three weeks; another in which flaccid paraplegia developed; and a third patient who was violently delirious. All these followed on intramuscular injection of 0·3 gm., in two cases twice daily.

In contradistinction to these, mepacrine seems in other cases to have a low toxicity, as in one recorded by MARKSON and DAWSON (p. 12) where a man took 25 gm. of the drug at once, after having had suppressive doses for the preceding 16 months. Vomiting and diarrhoea ensued after a few minutes, with collapse, stupor and contracted pupils. His condition improved on his being given an intravenous injection of 15 minims of 1/1,000 adrenaline and 5 mgm. of riboflavin (as a possible antidote) and 2 pints of 30 per cent. glucose by intravenous drip. Recovery was complete in a few hours. BURNHAM (p. 525) mentions a case of attempted suicide, where a man took 90 grains in a single dose; recovery was complete and there were no apparent signs of liver damage.

WILLIAMSON *et al.* (p. 1009) found that the toxicity of mepacrine for rats was enhanced when it was combined with a diet containing much calcium. Whether this is to be ascribed to increased absorption, decreased excretion, or to a specific effect of calcium on mepacrine metabolism, is uncertain. In this connexion the experimental work of FITZHUGH, NELSON and CALVERY (p. 525) with rats may be referred to. When the administration was kept up for long periods, the drug accumulated in the tissues, and signs of chronic poisoning were seen—leucocytosis, increase in red cells and in haemoglobin, inanition (which might end fatally in those on a low protein diet) and marked damage to the heart and liver.

MAEGRAITH, FRANKLIN, *et al.* (p. 905) have carried out some interesting work on the effects of mepacrine on the alimentary canal of man, which go far to account for the untoward symptoms sometimes complained of after its administration. The dose of mepacrine was followed 1½ hours later by a barium meal, and observations were made radiologically. After a single dose of 0·6 gm. and upwards, there were complaints of headache, nausea and there might be repeated vomiting, colic and diarrhoea, and, in some cases, rise of temperature with prostration. These symptoms might persist for 8–9 hours before becoming alleviated. Taking of the barium meal was succeeded by gastric hypersecretion, hyperperistalsis and increased tone of the pyloric antrum, succeeded by atony and pylorospasm. On entering the colon the meal advanced rapidly and there

was marked outpouring of secretion. With doses of 0·1 gm. daily none of these symptoms arose. During the war, some of the men receiving 0·2 gm. twice a week would complain of similar symptoms, and still more after three such doses in the week. The authors conclude that when a dose of mepacrine is repeated at intervals greater than two days, the tolerance for mepacrine in some of the subjects may be reduced by the time the third dose is given.

Some interesting accounts have been published on the use of mepacrine in combination with other drugs. For preventing relapses of benign tertian malaria FEDOTOV (p. 12) has found the following satisfactory: A minimum of three courses, each in a cycle of 3, 5 and 3 days, with ten-day intervals between the cycles and a month between the courses. For the first course he gives 0·3 gm. of mepacrine daily; for the second and third courses 0·2 gm. mepacrine together with 0·04 gm. pamaquin. Of those who received all three courses only 3·5 per cent. relapsed; 25 and 15·6 per cent. of those who had had only one or two courses. Of untreated cases relapses occurred in 25·8 to 98·6 per cent.

American troops who had been for about 6 months on Guadalcanal, a highly malarious island, were transferred to malaria-free Samoa. DOWNS (p. 1004) reports on the various forms of treatment there adopted and the conclusions reached in relation to *P. vivax* infection: namely, that few, if any, were cured of their infection by 0·4 gm. atebrin a week, which had been the suppressive method adopted during the time of their exposure on Guadalcanal; nor were they cured by mass therapy with atebrin, either alone or in combination with plasmoquine; initial attacks of malaria occurred up to six months or more after the suppressive atebrin had been stopped; lastly, there was a definite tendency to relapse in the fifth and sixth weeks after the first observed attack.

An interesting comparison was carried out by ROGAN and COOMBES (p. 524). They first investigated the efficacy of the "standard Army treatment" of troops in the field in Assam (quinine 30 grains daily for two days, mepacrine 0·3 gm. daily for 5 days, a rest period of two days, then pamaquin—0·02 gm. for Natives, 0·03 gm. for British troops—for five days). This was found to be quite efficacious, but they go on to record another series of observations made in an Indian General Hospital in Gauhati, Assam. Here, five methods of treatment were compared and were found to be almost equally effective. The recommendation was made to omit quinine and pamaquin from routine treatment which should consist of mepacrine only, with a moderately large initial dose, followed by suppressive mepacrine treatment.

Paludrine.—The team working at the Liverpool School of Tropical Medicine, in conjunction with Imperial Chemical Industries Ltd., on antimalarial drugs, has issued a comprehensive statement of the steps which led to the discovery of Paludrine (pp. 394–403). The chemistry of the various compounds, tested in birds and man, is too complicated to be described here, and details should be sought in the original abstracts.

This team (p. 396), after studying various synthetic antimalaria drugs, proceded to investigate the action of 3349, first on *P. gallinaceum* and then on human infections acquired in West Africa or the Mediterranean. Patients with subtertian malaria were given 0·2 gm. orally thrice daily for 7 days. Some had no relapse during the ensuing 3½ months of observation; others relapsed and were given a second course. Less than 0·2 gm. doses were found to be ineffectual. Sexual forms of the parasite are not affected by the drug. The results are comparable with those attained by 0·2 gm. mepacrine thrice daily for two days, followed by 0·1 gm. thrice daily for five days. This drug, 3349, though at times causing colic and diarrhoea, is preferred to mepacrine by many because it does not produce the yellow staining of the skin associated with the latter.

Clinical trials of the compound 4888 (Paludrine), which was developed from the earlier substances, showed very great success in the treatment of *P. vivax* and *P. falciparum* infections, and the drug was therefore sent to the Australian Army Research Unit for extended trial under the exacting conditions developed by that unit, under the Directorship of FAIRLEY (p. 527). With *P. falciparum* infection 25–100 mgm. were given daily, and the drug appeared to be a true causal prophylactic. With *P. vivax*, 100–300 mgm. daily suppressed the infection but did not prevent attacks after the drug had been discontinued. 100 mgm. daily protected against mixed sporozoite infections with *P. vivax* and *P. falciparum* in volunteers, even when they were subjected to strenuous exercise, chilling, and injection of adrenaline, so long as the dose was taken, but benign tertian attacks occurred within five weeks of the treatment being stopped.

For therapeutic purposes, in *P. falciparum* infections the standard course is 300 mgm. daily for ten days; in *P. vivax* infections dosage was varied from a single dose of 100 mgm. to 1·0 gm. daily for a fortnight. Relapses were observed after a period of freedom up to 86 days. Gametocyte production in *falciparum* infections is unchecked by the standard course of paludrine. Its mode of action is to affect the amoeboid forms, or at a later stage in schizogony. It has a powerful action on the maturing schizonts of *P. vivax*.

When paludrine is being given it is important to know the amount present in the blood. This usually ranges between 10 and 100 μgm. per 100 cc. KING, WOOTTON and GILCHRIST (p. 822) have described a modification of the method of SPINKS and TOTTEY (p. 400) for determining the blood level.

DAVEY, working for the Biological Department of the Imperial Chemical (Pharmaceuticals) Limited (p. 1010) has ably summarized the information on paludrine. Its suppressive effect is almost perfect; 25 mgm. daily completely suppresses malignant tertian, and 100 mgm. suppresses benign tertian. A single dose of 100 mgm. controls a clinical attack so that relapse does not take place for several weeks. In man, toxic symptoms may follow doses of 500 mgm. taken twice a day for four weeks, and single doses should not exceed 750 mgm.

A single dose of 100 mgm., or repeated doses of 50 mgm. bring about clinical cure of malignant tertian fever, and doses of 100 mgm. three times a day for ten days effect a radical cure. In benign tertian malaria these doses effect a clinical cure, but not a certain radical cure. Paludrine does not destroy gametocytes but renders them non-infective for mosquitoes for several days, probably by action of the drug while in the stomach of the mosquito.

Other Drugs.—A new drug, *Chloroquine*, SN 7618, a quinoline derivative, has been synthesized in the United States (p. 708) and has proved to be active in infections due to *P. vivax* and *P. falciparum* and in avian malaria. It is readily absorbed and slowly excreted. In properties it resembles mepacrine and its toxicity is similar, causing transient headache, visual disturbances, gastro-intestinal upset and pruritus. In benign tertian malaria it is an effective suppressant, but it is not curative or prophylactic. In malignant tertian it is effective in acute attacks and can bring about cure when given in doses of 0·6 gm. followed by 0·3 gm. in 6–8 hours and 0·3 gm. on each of two successive days. MOST and his colleagues (p. 1011) have also reported upon its use. They found that it freed the peripheral blood from parasites, abolished fever and controlled the symptoms generally better than either atebrin or quinine. In some patients it gave rise to general or localized pruritus, but this was usually transient. Relapses were slightly fewer than with atebrin or quinine. The general conclusion is reached that chloroquine is safe and highly effective and, judging by their results, superior to quinine or atebrin.

Vitaquine.—Success from the use of Vitaquine was reported by PERRET-GENTIL (p. 200). Vitaquine is a mixture of cinchona alkaloids with a vitamin C preparation.

Tonkin and Work (p. 1012) tested two Chinese plants with reputed anti-malaria properties, namely *Fraxinus malacophylla* and *Dichroa febrifuga* (chang shan), and Mukerji (p. 1012) tested the former of these and also two Indian plants, *Alstonia scholaris* and *Caesalpina bonducella*. The conclusion arrived at was that all four had a slight febrifugal action, but no true antimalarial effect, and consequently that their reputations rested solely on the former of these actions.

Heidelberger and his colleagues (p. 816) describe in detail their mode of preparation of vaccines and suspensions containing plasmodia. Those interested should consult the original; the process is too complicated to be detailed here. Attempts were made by their use to terminate relapses in chronic benign tertian infection; they have also been tested for prophylactic properties, and used for immunological studies.

The same authors (p. 1013) made several trials with a vaccine prepared from infected blood, in naturally contracted *vivax* malaria, in therapeutic malaria and against mosquito-borne *vivax* infection. No evidence was obtained of its conferring any protection.

Spector, Haviland and Coggeshall (p. 823), having observed that recurrence of *P. vivax* malaria ceased in a group of syphilitic patients who were receiving a course of mapharsen therapy, determined to test whether mapharsen and carbarsone in maximum tolerated doses, would eliminate this type of malaria infection; the results indicated that they were of no value.

A report that two Indians suffering from kala azar and relapsing malaria had no relapse while under prolonged treatment with urea stibamine prompted Stokes (p. 299) to try the effect of this drug in cases of relapsing malaria, but he found no evidence of its having any influence on the latter disease.

Coxon and Hayes (p. 406) tried sulphadiazine in the treatment of benign and of malignant tertian malaria. They conclude that it has definite anti-malaria properties, but its action is inferior to and slower than that of either quinine or atebrin, and it is followed by a much higher relapse rate.

Suppression.

Duncan (p. 708), who was with the United States Sixth Army Training Centre in Australia, investigated mepacrine as regards its suppressant activity; he found that success depended on the thoroughness of supervision and that 0·1 gm. daily on six days a week sufficed. Under combat conditions, when supervision was ruled out, 0·4 gm. twice a week proved the best dosage. Boyd and Kitchen (p. 304) confirmed the usual finding that the taking of 0·1 mgm. six days a week, begun a week before and continued through the period of exposure, gives complete protection against *P. falciparum*, but not against *P. vivax*; even when this dosage is continued for a fortnight after the period of exposure, *P. vivax* may become clinically active later, after prolonged incubation.

Untoward effects associated with the use of atebrin for purposes of suppression have been reported by several authors, particularly a condition which has been called the "atypical lichen planus syndrome," recorded in New Guinea, Assam and North Burma. Violaceous or eczematoid plaques appear, at first localized to the dorsa of the hands and feet and to the side of the neck, later becoming more widespread and even generalized; secondary pyogenic infection is common. Other cases of atebrin dermatitis have been noted by Whitehill (p. 303) and Nelson (p. 303). Tests carried out on negro soldiers by Gottfried and Levine (p. 301) led them to conclude that the drug, even after prolonged administration (0·1 gm. six times each week for 18 months) did not cause liver damage.

The Australian Army Medical Research Unit, under the directorship of Fairley (p. 628), tested the suppressive value of M 4430. This drug corresponds

closely to paludrine, M 4888, one H being replaced by CH_3. Doses of 200 mgm. were given daily; malaria was temporarily suppressed but developed at periods ranging between 16 and 59 days after the treatment was stopped; this is interpreted as indicating that the [postulated] exoerythrocytic forms were not eradicated, but that M 4430 acts as a partial prophylactic against *P. vivax* infections—at least as regards the New Guinea strains.

In connexion with suppression, reference may again be made to the report of MOORE (p. 4) on coloured and white American troops in Liberia, already mentioned in the Epidemiology section of this summary.

Control.

BEKLEMISHEV, SHLENOVA and ORLOV (p. 1112) have undertaken an important investigation—an estimation of the size of the area to be covered by antilarval measures for protecting a given site against malaria carried by *A. maculipennis messeae*. Their method was to ascertain the rôle of each concentric belt around the settlement upon the mosquito density of it. Estimation was made of the density of larvae in an area with a radius of 3 kilometres from the settlement, after which antilarval measures were undertaken in all breeding-places within three concentric zones in succession, each one kilometre in width. A centrifugal increase was noted in the second zone, but the density in the third zone was unable to keep pace with the losses caused by antilarval treatment of the first two. After treatment of the first zone, the mosquito density of the settlement was reduced by 82·4 per cent.; after treatment of the second zone it fell to 0·3–0·4 per cent. of the original density. Thus, larval destruction within a radius of two kilometres almost completely stopped the influx of active female mosquitoes into the settlement. Hence, a clearance of two kilometres is sufficient, but, in case some had merely been deflected to neighbouring villages or to cattle in the vicinity, it would, in some cases at least, be advisable to cover a radius of three kilometres.

The Public Health Department of the Portuguese Ministry of the Interior (p. 903) has issued a series of publications dealing with antimalarial work in that country.

FELTON, BARNES and WILSON (p. 308) have put on record the measures adopted in parts of the U.S.A. to protect those in non-endemic areas from infection present in men returned from malarious regions abroad. Mobile malaria units have been established, each unit consisting of a station wagon and a 1½ ton truck to carry material for entomological surveys, larvicidal operations, minor drainage, clearing and cleaning, and sprays for killing mosquitoes. Control measures are carried out wherever human carriers and the insect vector are concentrated. Fifty-seven areas were surveyed during 1943–44. *Anopheles quadrimaculatus* was present in 32 of them and the densities were generally high.

In spite of difficulties, such as shortage of antimalaria drugs, inadequate transport and obstacles to recruiting labour for carrying out antimalarial measures, COLLIGNON (p. 307) reports that the malaria situation in Algiers remained "not unsatisfactory"; in fact, the indices of infection were somewhat lower than in the two preceding years.

MAGOON (p. 877) has written a book in which, after presenting information on the epidemiology of malaria in the Caribbean area, he relates in some detail the engineering aspects of malaria control in mangrove swamps, flood plains and seepage areas, with an account of the necessary equipment and materials.

RIBBANDS (p. 1014) reports on the use of DDT in oil on running water, not as a continuous spray [see also p. 409], but in discrete applications; the anophelines were of Indian species. He found that in narrow streams, 2 ft. or so across and flowing 12–15 ft. per minute, 10 cc. of 5 per cent. DDT in waste

engine oil eliminated 97 per cent. of anopheline larvae through a distance of 100 yards. Over a river 30 ft. broad with an average flow of 75 ft. per minute a single application of two gallons of the same (5 per cent.) strength gave effective control for 2,280 yards. The same author (p. 409), and also DEONIER and BURRELL (p. 410) in America, have carried out more experiments, the former applying DDT in oil from an oil-can, the latter in solutions or emulsions or as a dust from an aeroplane. Ribbands found that 2 gallons of 5 per cent. emulsion per acre gave complete control for 11 days, 30 per cent. control to the 18th day, and even longer partially, whereas the oil without the DDT was quite ineffectual by the 11th day. By aeroplane distribution, preliminary tests gave kills from 94·9 to 100 per cent. in vegetated marshes and complete in open water. BUXTON (p. 305) tested the larvicidal effects, in the Gold Coast, of emulsions of 5 per cent. DDT in lubricating oil with an emulsifier, and compared them with those of a 5 per cent. concentration in a dieseline solution. The latter proved much superior: 0·01 cc. per sq. yard killed 100 per cent. of the larvae, and the effect lasted for two days; 0·02 cc. killed 80–100 per cent. and lasted for 2–3 days, whereas this quantity of the former emulsion was entirely ineffective and as much as 0·5 cc. per sq. yard was needed to bring about a kill of 95–100 per cent., but the effect lasted for ten days.

COTTAM and HIGGINS (p. 1014) investigated the effect of DDT in solution or emulsion, on fish and wild life in the United States; they found it lethal to crabs and fish, and they, therefore, advise against its being used in streams, lakes and coastal bays; but each case must be considered on its own merits, because, if this generality were followed, the use of DDT in mosquito control would be sadly hampered, for in many places where DDT is needed aquatic life is negligible or unimportant.

JOHNSON and EASON (p. 1111) report promising results from the use of pellets of DDT in water collections in America. The pellets were prepared by melting paradichlorobenzene and adding solvents containing DDT and emulsifiers, and DDT in crystalline form. They give in their paper seven formulae. During the first six weeks the larvae present were markedly reduced, but after that time scum and vegetation impeded its action.

Larvicidal applications to rice-fields are limited and liable to prove expensive because of damage to the growing rice. KNOWLES and FISK (p. 529) have shown that addition of DDT in a concentration of 1 p.p.m. to the flowing water entering the rice-fields will reduce the breeding of *A. quadrimaculatus* (0·2 p.p.m. will suffice for Culicines), but will not eradicate them; the rice is not injured thereby. ANANIAN and his fellow-workers (p. 13) have shown that mosquitoes in rice-fields in the Caucasus can be controlled by intermittent irrigation—flooding for 8 days and drying for 5 days.

DDT as a mist from an aerosol cylinder has been found by JONES and his colleagues (p. 530) to be lethal to larvae of *A. quadrimaculatus* to a distance of 60 feet. Field tests confirmed the practical value of the method, full control resulting from the use of 0·1 lb. per acre on swamps of up to 9,750 sq. feet.

METCALF and his colleagues (p. 102) found that DDT does not debar *Anopheles quadrimaculatus* from entering a treated room, but fully 95 per cent. receive a lethal dose before they leave it again and the chain of transmission is thus broken. Dispersion from aircraft presents difficulties; when in a concentration above 5 per cent. in inert dust it tends to cake and the use of kerosene as a diluent entails a heavy load, but 15–40 per cent. solutions in "certain polymethyl naphthalenes" sprayed from a special apparatus gave 90 per cent. kills over a swath 200–300 ft. wide, with doses of DDT less than 0·03 lb. per acre.

SCHARFF *et al.* (p. 203) in reports from the Medical Advisory Division, South-East Asia Command, have recorded the results of the use of DDT for indoor

spraying and air-spraying trials. For details the originals should be consulted, but it may be stated here that DDT remaining in vegetation killed mosquitoes newly hatched and those coming to oviposit.

Simmons and his staff (p. 104) tested the effectiveness of DDT in control of *A. quadrimaculatus* in a series of laboratory and field experiments, using various strengths of DDT in various solvents—" Triton X-100," " Duponol OS," " Arctic Syntex A " and others. When DDT is used as a larvicide, 90–95 per cent. of the kill takes place within the first hour and the residual effect wears off in a few days, though the subsurface water remains toxic to larvae for longer. For other details those interested should consult the original paper.

Cambournac and Simões (p. 306) tested the larvicidal potentialities of the two DDT preparations: Neocid and 7013 Geigy [the composition of this is not given]. The results of their action were not consistent and any larvicidal action was of brief duration.

Deonier *et al.* (p. 101) found that, comparing DDT as a dust with Paris green, 0·005 lb. of the former per acre gave 100 per cent. kill of larvae of *A. quadrimaculatus* in 48 hours, while 0·1 lb. of the latter gave only an 85 per cent. kill in the same time. Moreover, the former was resistant to sinking, even after rain. Such were the results in laboratory trials. In the field 0·05–0·1 lb. of DDT per acre gave 100 per cent. kill, but had no residual action. For residual effect as much as 1–2 lb. per acre and a 20 per cent. mixture, were needed. Colloidal suspensions were very promising, giving 94–100 per cent. kill up to three months, but high concentrations killed fish as well as the aquatic insects.

Price and Lyman (p. 14) found dusting by Paris green from an aeroplane a very effective method of controlling the breeding of *A. quadrimaculatus* in the Potomac River.

Gahan, Lindquist, Travis and Morton (p. 99) carried out series of tests on the control of *A. quadrimaculatus* by DDT, first in the laboratory, then in small-scale, later in large-scale field work. They found that concentration of chemical in the spray used does not materially affect the toxicity of the residue, so they used 2·5 per cent. as a standard. Unpainted surfaces treated with this remained lethal for as long as a year, but the " knock-down " time increased from an initial two hours to as much as five hours in films 32 weeks old. On painted surfaces 100 per cent. kill was recorded 32 weeks after the application of 50 mgm. per sq. foot, if the surface was coated with cold water casein paint. On oil paint surfaces the duration was much shorter, not more than a week, and the knock-down after five hours was reduced to one-fourth. Anopheline counts in houses, for four months after the end of treatment, compared with adjacent control areas, showed a reduction of 99 per cent. when 208 mgm. per sq. foot had been used and 91 per cent. when 56 mgm. had been applied.

Control in rural areas, houses occupied by plantation negroes, is reported upon by Knowles and Smith (p. 710). A stock solution containing DDT 23 per cent., xylol 71 per cent. and Triton X-100 6 per cent. was prepared and diluted with water to give emulsions of strengths 5, 2·5, and 1 per cent. DDT. The percentage reduction of *A. quadrimaculatus* one to two months later was 88 with 5 per cent., 74 with 2·5 per cent., and 66 with 1 per cent.

Senior White (p. 306), in the hyperendemic Jeypore Hills, compared the results of house spraying with DDT and with pyrethrum extract, the local infection being by the *fluviatilis* group. He concludes that DDT is more effective, and very much cheaper, than pyrethrum.

Deonier and Jones (p. 531) have compared a new compound, TDE, with DDT as regards toxicity to larvae of *A. quadrimaculatus*. TDE contains two chlorine atoms in the ethane nucleus, instead of the three of DDT. TDE appeared to be slightly the more toxic.

Benzene hexachloride has been tested by LOZANO MORALES (p. 205). Excellent results were obtained by using it in powder form, one per cent. mixed with road dust, in *Anopheles* breeding-places. It can also be used as a suspension in water.

THOMSON (p. 93) has written a paper, very informative statistically and geographically, on the breeding-places and control of *A. melas* in coastal parts of Sierra Leone. Breeding occurs in association with *Avicennia nitida* and *Paspalum* (sea-grass) on ground between neap-tide and high spring-tide levels. Oviposition in *Avicennia* orchards takes place on the earliest of the spring tides and the eggs are distributed widely by tidal action. When the spring tides subside some of the eggs are left in pools in which they develop; others are stranded in mud where they survive until the next tide floats them, when they immediately hatch out. Thus, output of adults is periodic, occurring in waves after the end of the spring tides. In *Paspalum* areas egg-laying occurs at any time. The periodicity and output of adults accordingly depend on the occurrence of spring tides and *their* periodicity, on there being enough rain to prevent the drying up of pools left by the spring tides, and on the presence of seepages maintaining tidal pools. Control by drainage is not effective because opportunities for oviposition and persistence of pools inevitably occur after spring tides. To eliminate breeding, embankment to exclude the spring tides from *Avicennia* and *Paspalum* areas, and drainage of fresh water through tide gates, have proved quite successful.

VINCKE and PARENT (p. 307), procured marked reduction of *A. gambiae*, the chief vector of malaria in Stanleyville, by oiling, filling and drainage. But there has been no diminution in the parasite rate in children.

MUSPRATT (p. 704), finding that fungi of the *Coelomomyces* genus are parasitic in larvae of *A. gambiae* in Northern Rhodesia, causing a mortality of some 95 per cent. of them, suggests their possible use in the biological control of this vector.

According to BERBERIAN (p. 1105), of the eight species of *Anopheles* captured in Syria and Lebanon, the important vectors are *A. sacharovi*, *A. superpictus* and *A. claviger*. The first breeds in inland and coastal swamps and in springs, pools and cisterns, and in winter settles in houses, barns and stables, emerging on warm days to feed and then returning to their hiding-places; the second transmits much of the rural malaria, especially in the coastal belt; the third breeds in wells. For control the hiding-places of the two former should be sprayed with 5 per cent. DDT emulsion in December or January and March, followed by antilarval measures; for controlling the third, wells and cisterns should be sprayed every two months.

GILLETTE (p. 824), reports that *A. aquasalis* and *A. bellator* are the chief malaria vectors in Trinidad, and the former of these in Tobago. Animal barriers are serviceable against *A. aquasalis*, but effective control has been obtained by construction of a culvert with a sea head to keep the mouths of small streams open and by automatic flushing siphons. The breeding-places of *A. bellator* in Bromeliads were satisfactorily dealt with by spraying with 0·5 per cent. copper sulphate solution.

AFRIDI and ARTHUR (p. 204), give an account of the incidence of malaria and its control on the Indo-Burma front in 1942–44. Malaria rates were high at the beginning of the campaign. Later, mepacrine, DDT and the use of head-nets ($\frac{3}{8}$ inch mesh) impregnated with dimethyl phthalate, afforded personal protection.

PHILIP, RAMAKRISHNA and RAO (p. 203) observed in Madras that spleen rates were higher in boys than in girls, and ascribed this to the fact that the girls anoint themselves with turmeric and vegetable oils. Experimentally, in cages, turmeric and mustard oil repelled hungry *Anopheles* of several species,

but, as BUXTON points out, it is not safe to conclude from cage experiments that the same means would be effective under ordinary living conditions.

Therapeutic and Inoculation Malaria.

Inoculation malaria is usually much more severe in white than in coloured patients, but convalescents from artificially induced *P. falciparum* infections usually exhibit clinical tolerance when re-inoculated with a heterologous strain; there is a shorter period of clinical activity. White patients re-inoculated thus react like coloured patients on primary inoculation—one wave of trophozoites followed by a wave of gametocytes. Gametocyte production is often greater after heterologous re-inoculation, in the case of coloured patients, than it was after the primary infection. Hence, it would seem that the immunity acquired during convalescence from a *P. falciparum* infection has an appreciable heterologous value (BOYD and KITCHEN, p. 1003).

CIUCA and his colleagues (p. 292) kept under observation for 4 to 14 years 41 patients who had been subjected to malaria therapy. Their immunity was tested either by determining persistence of the parasites, by transfusion of blood into a susceptible individual, or, directly, by a fresh injection of virulent blood. *P. malariae* conferred the most lasting immunity, *P. falciparum* the shortest. The same authors (p. 290) studying *P. falciparum* gametocyte carriers, some being cases of natural infection, others artificially infected with virulent blood or with sporozoites, found that the infectivity of the naturally infected carriers was higher than that of the others; the vitality of the gametocytes of the naturally acquired strains appeared to be much higher than those of the therapy strain.

BOYD (p. 289) tells of difficulties in maintaining propagation of *P. falciparum*; even when sporozoites are present in the mosquitoes, but they may fail to infect. Resistance on the part of the patient does not account for it, for subsequent inoculation may succeed; it is not due to age of the sporozoites, for quite young ones may fail. A possible explanation is that if the patient from whom the mosquitoes gain infection has recently taken quinine, this may impair the vitality of the resulting sporozoites.

A. quadrimaculatus allowed to feed on patients with *P. vivax* infection acquired in the Pacific showed an infection rate of 11·8 per cent. (WATSON, p. 290), and the highest rate was obtained in mosquitoes which had fed on patients who had parasitic relapse but no fever.

KAPLAN, READ and BECKER (p. 1110), as a result of their investigation of the action of Thiobismol on blood-induced infections with *P. malariae*, found the drug of value in reducing the frequency of paroxysms and in controlling irregular cycles; it should, therefore, aid neurosyphilitics to tolerate a full course of therapy with this parasite.

Finally, FREDERICKS and HOFFBAUER (p. 97), studying the hepatic function in patients undergoing malaria treatment, conclude that such therapy is contra-indicated where there is clinically manifest disease of the liver.

Malaria other than Human.

Sporozoites of chicken malaria rapidly lose vitality when kept at room temperature. BRACKETT and HUGHES (p. 15) have found that to retain vitality the ground-up mosquito material should be chilled as soon as possible and kept in an ice-bath during the inoculations; infections produced are then more uniform. Exposure to room temperature even for 15 minutes probably results in marked injury to the parasites.

P. lophurae infection in chicks is more severe when the birds are on a diet deficient in folic acid, according to SEELER and OTT (p. 412), but passage through chicks on a deficient diet does not increase the actual virulence of the

plasmodium, because, on inoculation into normal chicks on an adequate diet, no enhancement of virulence could be detected.

WOLFSON (p. 716) has shown that rapid passage is a satisfactory method of adapting a parasite to a host only slightly susceptible on first transfer. A strain of *P. relictum* sent to America from England in young canaries produced only a mild infection in ducks at first but increased markedly in virulence after 40 semi-weekly transfers.

COULSTON, CANTRELL and HUFF (p. 205) in an article on the distribution and localization of sporozoites and pre-erythrocytic stages, in the tissues of fowls infected with *P. gallinaceum*, have shown that dispersal of sporozoites probably takes place by way of the blood-stream.

SPECK, MOULDER and EVANS (p. 1116) contribute another paper to their series dealing with the biochemistry of *P. gallinaceum*. This, the fifth, is concerned with the mechanism of pyruvate oxidation in the parasite. For more detail on the subject the reader is referred to previous issues of this *Bulletin*: 1938, v. 35, 709; 1940, v. 37, 190, 509; 1942, v. 39, 397, 742; 1943, v. 40, 674, and, more particularly, 1945, v. 42, 448, 967. The same authors have written also on the nitrogen metabolism of this plasmodium.

WOLFSON (p. 714) investigated the question of survival of three species of avian parasite, *P. cathemerium*, *P. lophurae* and *P. relictum*, when blood from infected ducks is rapidly frozen, then, after storage at —76°C. for periods of two hours to a year, rapidly thawed at 42°C. There was little difference between them as regards ability to survive, but the first-named survived more regularly than did the others. Inoculation into ducks produced a lower degree of parasitism than in controls inoculated with unchilled parasites, but one to three subsequent passages usually restored the virulence of the former.

JACOBS (p. 206), after a series of attempts to increase the resistance of ducklings to infection by *P. lophurae* by previous injections of materials containing the Forssman antigen, or hapten, prepared from guineapig kidneys, horse kidneys and sheep erythrocytes, met with practically no success; the results were largely negative. As the result of experiment on ducks, ROSTORFER and RIGDON (p. 309) believe that anoxia plays an important part in bringing about death from acute malarial infections.

Studies of some importance have been taken up regarding immunity in avian (and to a less degree in monkey) malaria. Thus, HUFF and COULSTON have published an informative paper on the relation of natural and acquired immunity of chickens, geese and ducks to the cryptozoites and metacryptozoites of *P. gallinaceum* and *P. relictum*. The work cannot be further abstracted here; those interested should turn to the full abstract in this *Bulletin* (p. 1115) or to the original.

TALIAFERRO, TALIAFERRO and SIMMONS (p. 629) have demonstrated that X-irradiation in *P. lophurae* infections on the day of injection results in fatal infection; at other times it causes only slight relapses. The effectiveness of the X-rays varied with the age and susceptibility of the chickens, the species of parasite (*P. gallinaceum* was also tested), the stage and intensity of the infection. These variations seem to be related to natural and acquired immunity, which is modified by the destruction of lymphocytes brought about by irradiation.

Antibody production is increased and more durable if the antigens are combined with Falba (a lanoline-like substance) and paraffin oil. FREUND *et al.* (p. 311) have attempted to immunize young ducks against *P. lophurae*, and subsequently *rhesus* monkeys against *P. knowlesi*. Details of their experiments are too complicated to be given in the present summary, but the conclusion arrived at was that the ducks so treated had developed considerable resistance to subsequent infection with *P. lophurae*. In the case of *P. knowlesi* infection, the parasitaemia was modified and fatal results of infection prevented.

Advances have been made in the treatment of avian malaria, and DAVEY (p. 712) has investigated the activities of various drugs, according to the route of administration, intravenously or orally, and also the use and value of avian malaria for discovering and testing drugs for the treatment and prevention of human malaria.

MARSHALL, P. B. (p. 97) found, by testing their effect on *P. gallinaceum* infections, that quinine degradation products, for example an extract in which the quinine had been metabolized, lost thereby their antimalarial properties. DEARBORN and MARSHALL, E. K. (p. 404) have also investigated the degradation products of quinine in animals, when administered by the drug diet method [see this *Bulletin*, 1943, v. 40, 223] or intravenously to ducks and chicks, and by the latter route to dogs. The authors conclude that there are probably at least two degradation products to be found in the duck after administration of quinine, and that the degradation is similar, qualitatively, in the other animals.

FUNKE, BOVET and MONTÉZIN (p. 713) have synthesized a quinoline derivative 2236F. Tested on canaries infected with *P. relictum* it had a therapeutic index of 1/50. The authors suggest that, as its toxicity is low, it should be tried clinically in human malaria.

Sulphonamide drugs vary in their absorbability and in their action upon the malaria parasites of birds. The concentration in the red cells is usually higher in the canary than in the chick, but the action is much less. A blood concentration of 10 mgm. sulphadiazine per 100 cc. was found to be very active against *P. gallinaceum*, but 60–100 mgm. per cent. were needed to suppress *P. cathemerium*, and the degree of antimalaria activity in chicks is correlated with the height of the blood concentration curves (MARSHALL, P. B., p. 15).

BRACKETT, WALETZKY and BAKER (p. 411) have determined that the rate of action of slowly acting antimalaria drugs, as sulphadiazine, increases in proportion with the slowness of the rate of growth of the organism, a matter which may have an important bearing on chemotherapy. The same investigators (p. 713) have compared the action of sulphadiazine with that of quinine on *P. gallinaceum*. Whereas quinine acted almost immediately, arresting development of the parasite, with sulphadiazine the first signs of retardation of development were seen between the 12th and 24th hours, and the first treated generation of parasite went on to segmentation and invasion of fresh erythrocytes. Thus, in chickens treated with quinine, there was never any increase in the number of parasites in the blood, whereas with sulphadiazine there was a fourfold increase in the first two days.

BOVARNICK, LINDSAY and HELLERMAN (pp. 824–6) have reported on their studies of the metabolism of *P. lophurae*, undertaken to obtain information on the mode of action of antimalarial drugs. They found that atebrin inhibits glucose oxidation in parasites depleted of substrate and its action may be due to interference with some phosphorylation reaction before glucose can be utilized. Adenylic acid was found to be antagonistic to the action of atebrin.

SEELER, MALANGA and PIERSON (p. 309) tested the action of streptomycin on *P. cathemerium*, *P. lophurae* and *P. gallinaceum* in Leghorn chicks, infected by intravenous inoculation of infective blood and, in the case of *P. gallinaceum*, of sporozoites also. The doses given were 25,000 to 400,000 units intramuscularly per kilo. body weight per day. The streptomycin was found to exert a slight suppressive action on infection induced by sporozoite inoculation, but none in blood-inoculated infections.

EXEMPLARSKAYA (p. 1113) finds that the treatment of monkeys infected with *P. inui* by means of "cytotoxic antireticular serum", prepared by immunizing an animal with an emulsion of the reticulo-endothelial tissue of

another, leads to stimulation of the defence phagocytic function of the reticulo-endothelial system in infected monkeys, resulting in a suppression of all manifestations of the infection.

Lastly, KNISELY and his colleagues (p. 1113) have prepared a film showing the normal physiology of the blood of *rhesus* monkeys and of those suffering from *P. knowlesi* infection, and demonstrating the changes that occur leading to clumping of the red cells, impeding of the circulation, and so to anoxia. The effect of atebrin in disintegrating the clumps is also shown. The film can be borrowed by medical schools, medical societies, the Services and research groups. *H. Harold Scott.*

MALARIA.

SINTON, J. A. **Malaria in War.** Reprinted from *Ulster Med. J.* 1946, May, 28 pp., 7 charts. [22 refs.]

This "Robert Campbell Memorial Oration" covers familiar ground in a very interesting manner. Records of malaria in military history are drawn on to illustrate the important part malaria has played in determining the fate of armies. An admirable summary of antimalaria measures leads to a description of the progress in the prevention and control of the disease achieved in response to the stimulus of the late war. *Norman White.*

GÓMEZ MARCANO, A. Sugerencias para los que trabajan sobre indices esplenicos. [**Suggestions for those working on Splenic Indices.**] *Tijeretazos sobre Malaria.* Venezuela. 1946, Mar., v. 10, No. 1, 3–19. [11 refs.]

For the benefit of medical officers engaged in the determination of spleen indices the author discusses at length matters of detail, some small but none the less important, which should be taken into consideration. His own practice is to determine spleen indices during the months of January to May inclusive, the dry season when malaria transmission is at its lowest or non-existent. The sample of the population submitted to examination demands careful consideration. In the examination of schoolchildren the place of residence, race, age, sex, and the economic and nutritive state of the individuals should always be recorded. The size of the sample examined is of great importance. In communities of 4,000 inhabitants or less, the number of children examined should not be less than 10 per cent. of the population; in practice this means the examination of the total school population. Towns with a population of from 4,000 to 8,000 are divided into four areas and 100 children from each quadrant are examined. In larger towns, chief attention is paid to children living near the periphery where malaria is likely to be much more prevalent than in the centre of the town.

Not all enlarged spleens are palpable, and spleens palpable only on inspiration are sometimes difficult of interpretation. Where the latter are predominant, the determination of the parasite index is important. In certain parts of Venezuela schistosomiasis is a cause of splenomegaly. *Norman White.*

JADIN, L. B. & HERMAN, F. Paludisme de montagne et action du sulfate de quinine brut sur la malaria. [**Malaria at High Altitudes and the Action of Crude Quinine Sulphate on Malaria.**] *Ann. Soc. Belge de Méd. Trop.* 1946, June 30, v. 26, No. 2, 111–16.

The authors report a marked extension of endemic malaria during recent years in the hills of Ruanda. As a precaution against famine, natives of

Ruanda-Urundi have been compelled to cultivate parcels of land in the valleys. This has entailed primitive irrigation work which has provided facilities for mosquito breeding that were absent before. Malaria in and around Astrida, alt. 1,750 metres, is now very prevalent (parasite rate 38·8). The anophelines found in order of prevalence were : *A. christyi*, *A. de Meilloni*, *A. squamosus* var. *entebbiensis*, *A. coustani*, *A. funestus* and *A. gambiae*. The last two species are the only recognized vectors but the rôle of *A. christyi* remains to be studied in this region.

Locally manufactured crude quinine sulphate prepared from locally grown Cinchona has been used with success in the treatment of malaria. This crude preparation contains 90 per cent. of the quinine salt. *Norman White.*

VISWANATHAN, D. K. **The Seasonal Prevalence of Malaria transmitted by *Anopheles fluviatilis* James 1902 in Different Regions of Bombay Presidency.** *J. Malaria Inst. of India.* 1946, June, v. 6, No. 3, 253–7. [11 refs.]

Data compiled by the staff of the Malaria Organization of the Bombay Presidency reveal that the transmission season in the *fluviatilis* malaria tracts is determined by the availability of breeding grounds for *A. fluviatilis*, such as streams and channels, rice fields, uncultivated swampy fields, sugar cane and betelnut-garden trenches and shallow earthen field wells. The author has divided these malaria tracts into four regional groups, each with its particular transmission season ; the heavy rains occur between June and September. In Group One, the heavy seasonal rainfall (over 100 inches per annum) flushes out the perennial streams, the large natural channels and the man-made betelnut-garden trenches in a region of narrow, deep valleys ; in consequence the transmission season is December to June.

In Group Two, natural and man-made channels in a rice and sugarcane area are well flushed by the seasonal rains (about 100 inches per annum), but in the absence of perennial flow of streams the season of transmission is restricted to October to December.

In Group Three, valleys of medium width and slope have perennial streams and man-made channels flushed only in the period of seasonal rains (about 100 inches per annum) ; steady transmission occurs, therefore, between October and June.

In Group Four, a region of broad valleys with extensive rice tracts, there is a low rainfall of 40–60 inches per annum ; conservation of water in tanks and a man-made irrigation system results in restriction of *fluviatilis* breeding to the period July–August to November.

By this regional grouping it is possible to concentrate control activities and transfer trained personnel from one region to another as required.

R. Ford Tredre.

PERRY, W. J. **Observations on the Bionomics of the Principal Malaria Vector in the New Hebrides-Solomon Islands.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, June, v. 5, No. 2, 127–39. [10 refs.]

The principal malaria vector referred to in the title of this paper is the form of *Anopheles punctulatus* now known as *farauti*.

Though accurate infectivity studies are lacking, malaria rates among members of the military forces in places where this is the only anopheline are sufficient to incriminate it. Typical *punctulatus* has been taken in small numbers ; though it feeds readily in captivity, it does not often do so in nature. However, in New Guinea *punctulatus* is known to bite man freely in nature and is regarded as a malaria vector.

Filarial infection in *farauti* in New Hebrides (Espiritu Santo) ranged up to 45 per cent. and in the Solomons (Guadalcanal) up to 52 per cent.

The summary of breeding places of *farauti* is taken from observations made in low lying coastal and inland areas by forty entomologists over a period of two years. In the " dry " season, rivers, streams, ponds, lagoons, taro gardens, ditches and wells are the main breeding places. In the " wet " season, all waters, natural and " man-made " are used. Hoof-prints and other small depressions are dangerous at this time. Breeding in artificial containers is not common. Water may be clear or turbid, brackish or fresh. The larvae are always to be found exposed to sunshine ; they need protection from currents and wind, such as is provided by *Spirogyra*, *Lemna* and *Myriophyllum*. Larvae are not usually found along the banks of rapid rivers and have never been taken in axils of plants. Under ideal field conditions, development from egg to adult takes about 7–10 days and breeding goes on all the year round, though in reduced numbers in the " dry " season.

Adults readily enter any shelter and remain for some time after feeding. Indoors, they are often found in pots, pans and other receptacles on the floor. Outside, the natural resting places have not been definitely located. The usual biting time is between 5 and 10 p.m., though there are some records of daytime biting. Even in the absence of human hosts, *farauti* may be abundant in an area ; for example, Russell Island had been uninhabited for over a year yet *farauti* was found breeding abundantly and feeding probably on animals.

Flight is probably no more than three-quarters of a mile from the breeding place. Eggs may be laid on mud and they and the larvae and pupae can withstand partial drying. Unmated females have been kept alive on fruit juice for 25 days and blood-fed females lived for 51 days. Males lived an average of 12·5 days (maximum 19 days). *H. S. Leeson.*

FLETCHER, O. K., Jr. **Apparent Anomalies in the Behavior of Anopheline Mosquitoes in Southwestern Georgia.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, June, v. 5, No. 2, 147–50.

While there is a wealth of information published regarding the specific aquatic requirements for the breeding places of United States anophelines, *Anopheles quadrimaculatus*, *A. punctipennis* and *A. crucians*, it is important that inexperienced field workers should realize that larvae of these species are sometimes found in unusual places. Instances are quoted of larvae occurring in such containers as rain-water barrels, concrete mixers, bird baths, watering troughs and so on. The possibility must not be overlooked and though such exceptional breeding places may be considered by some to be of no more than academic interest yet in certain circumstances they merit attention.

H. S. Leeson.

SABROSKY, C. W., MCDANIEL, G. E. & REIDER, R. F. **A High Rate of Natural Plasmodium Infection in** *Anopheles cruzians*. *Science*. 1946, Sept. 13, 247–8.

Existing information would lead one to think that *Anopheles crucians* is a very minor vector of malaria, though natural infections have been reported.

In 1945 dissection was carried out along a coastal swamp in South Carolina. There was a considerable amount of malaria [presumably benign tertian] : 7 to 10 per cent. of thick films were infected in autumn. In *A. quadrimaculatus*, the general vector in the U.S.A., gland infections were found in only 0·175 per cent. (in over 18,000 dissected). In November, *A. crucians* was found infected (3·38 per cent. in 701), and the infections tended to be high. Moreover at that

season, though *A. quadrimaculatus* had gone into complete hibernation, *A. crucians* was still feeding actively.

It is clear that *A. crucians* may yet prove to be a serious vector in Southern U.S.A., especially in spring and autumn. *P. A. Buxton.*

MAEGRAITH, B. **The Malaria Patient.** *Practitioner.* 1946, Aug., v. 157, No. 938, 81–92.

This article was written to assist the medical practitioner, with little experience of malaria, to recognize that disease and the complications that may attend it. The treatment of malaria is also outlined. *Norman White.*

EINHORN, N. H. & TOMLINSON, W. J. **Estivoautumnal** (*Plasmodium falciparum*) **Malaria. A Survey of Four Hundred and Ninety-Three Cases of Infection with** *Plasmodium falciparum* **in Children.** *Amer. J. Dis. Children.* 1946, Aug., v. 72, No. 2, 137–71, 2 charts. [Refs. in footnotes.]

During a six-year period children suffering from malaria admitted to the children's wards of the Gorgas Hospital, Ancon, and the Colon Hospital, Cristobal, Canal Zone, numbered 845 of whom 493 had *P. falciparum* infections, 334 *P. vivax*, 10 *P. malariae*, and 8 mixed infections. This paper is confined to a consideration of the *P. falciparum* infections. Cases occurred in every month of the year but were most numerous at the beginning and end of the rainy season which extends from May to December. Eighty-five per cent. of the cases came from unsanitated rural or semirural communities : infection is much commoner among mestizo than among white children. About one-fifth of the children in Panama have had at least one attack of malaria before the end of the second year of life.

In attacks of *P. falciparum* malaria in children, prodromal symptoms are frequent ; the cold, hot and sweating stages are ill-defined ; the chill is replaced by vomiting or convulsions in about half the cases ; the temperature is irregular or more or less continuous ; delirium, stupor, coma, muscular twitchings and convulsions are common. Thirty-eight per cent. of these patients suffered also from intestinal helminthiasis, Ascaris, Trichuris, strongyloides and the hookworms being most commonly observed.

The case mortality rate was two per cent. : 80 per cent. of the deaths occurred within 24 hours of admission to hospital.

Mepacrine is as effective as quinine in treatment ; the dose of mepacrine should be based on the weight rather than on the age of the child.

Norman White.

RYDER, J. B. & TOWSON, R. T. **A Case of Cerebral Malaria in Great Britain.** *Brit. Med. J.* 1946, Nov. 30, 815–16.

Cerebral malaria as a cause of coma in Great Britain is said to be rare and a search of the literature has revealed only two cases in recent years. A typical case is recorded in a steward of the Merchant Navy who had arrived four days previously from West Africa after a voyage of ten days. After being treated for influenza he had suddenly lapsed into coma.

The main theme of the paper concerns differential diagnosis.

Meningitis. The frequent occurrence of signs of meningeal irritation in cerebral malaria may confuse diagnosis.

Alcoholic Coma. Cerebral malaria often closely simulates alcoholism.

Cerebral Vascular Accident. (*a*) Subarachnoid haemorrhage. In this condition severe headache followed by rapid onset of stupor is characteristic and

meningeal irritation is well marked. The diagnosis is readily established by lumbar puncture. (*b*) Cerebral haemorrhage, thrombosis or embolism; but it is realized that embolism by malaria parasites may lead to peripheral manifestations.

Uraemia. The most likely causes of this condition in young adults are malignant hypertension or the alkali treatment of peptic ulcer with renal insufficiency. The onset of coma may be dramatic, but examination of the urine, blood urea and alkali reserve should differentiate this condition.

P. Manson-Bahr.

VAN LAERE, J. Contribution à l'étude de l'encéphalomyélite malarique. [**Malarial Encephalomyelitis.**] *Rev. Belge Sci. Méd.* 1942, Mar., v. 14, No. 3, 65–78, 11 figs. on 4 pls. [27 refs.]

Occurrence in a mother and her child.

SHUTE, P. G. **Antimalarial Drugs.** [Correspondence.] *Brit. Med. J.* 1946, Dec. 21, 966.

This letter relates to two previous notes in the *British Medical Journal*; one from Dr. HAMILTON of Assam (1946, Oct. 26, 638) who challenged the degree of success claimed for some antimalarial drugs and stated that results varied in different areas; the other from Dr. Ryan MACMAHON (1946, Nov. 30, 844) who suggested that differences in the composition or condition of batches of the drugs provided one explanation of their varying efficacy.

The present author refers to an article by JAMES, NICOL and himself published in 1932 [this *Bulletin*, 1932, v. 29, 693], and points to two important factors in assessing the effects of antimalarial drugs. Firstly, it has been proved that there are geographical strains within a species, and that they vary in clinical virulence. Secondly, a much larger total quantity of the drugs is required to cure a primary attack than is necessary for relapses or reinfections by the same strain of parasite, especially if treatment is not begun until the patient has had several days of fever; the smaller doses required for successive attacks might be explained by the presence of increased immunity already acquired.

These factors would explain the belief held in some quarters that antimalarial drugs vary in efficacy.

The author illustrates his first point by quoting the example of Rome and Sardinian strains of *P. falciparum*, which required for their control eight times as much quinine as was necessary in the case of two Indian, two West African, one Tanganyika and two Rumanian strains.

These results are shown statistically in the following table:—

	Total of Quinine, in gr. (and g.) during a Primary Attack	Total of Quinine, in gr. (and g.) during the Whole of the Course	Average per Case during Primary Attack, in gr. (and g.)	Average per Case during Whole Course in gr. (and g.)
Indian and other strains. No. of cases treated: 19	772 (50·2)	2,233 (145·1)	40 (2·6)	117 (7·6)
Rome and Sardinian strains. No. of cases treated: 13 ...	4,343 (282·4)	21,894 (1423·1)	335 (21·8)	1,680 (109·2)

H. J. O'D. Burke-Gaffney.

BROWN, M. & RENNIE, J. L. **Suppression of Benign Tertian Malaria with Mepacrine : an Investigation of 247 Cases of Apparent Failure.** *Ann. Trop. Med. & Parasit.* 1946, July, v. 40, No. 2, 190–98, 2 figs.

These observations concern 247 cases of *P. vivax* malaria that occurred in Italy among men who were supposed to be taking 0·1 gm. of mepacrine a day. One hundred and seventeen patients were suffering from a primary attack ; 100 were suffering from the second to fourth attack ; 18 from the fifth to seventh attack ; and 13 from the eighth or more. Seventy-three per cent. of the patients admitted that they had not taken mepacrine regularly. The mean plasma mepacrine concentration in 200 of these patients was 7·5 μ gm./1,000 ml., S.E. [Standard Error] 0·45. In a control group of healthy persons who were known to have taken the full suppressive dose of mepacrine it was 25·3 μ mg./1,000 ml., S.E. 1·92. The low plasma concentration in the malaria cases was not due to an abnormal excretion of mepacrine by the kidneys. Failure to take the drug regularly was the chief cause of its apparent failure to suppress malaria. *Norman White.*

LEVINE, H. D. & ERLANGER, H. **Atabrine and the Electrocardiogram.** *Amer. J. Med. Sci.* 1946, Nov., v. 212, No. 5, 538–40.

" In a series of 179 individuals atabrine in therapeutic and suppressive doses had no significant effect on the electrocardiogram. Abnormalities observed in patients receiving atabrine can be attributed to other causes."

WILSON, D. J. **Eczematous and Pigmentary Lichenoid Dermatitis : Atypical Lichen Planus ; Preliminary Report.** *Arch. Dermat. & Syph.* 1946, Oct., v. 54, No. 4, 377–96, 10 figs.

This report does not add much new material to our knowledge of this malady, but *inter alia* the histological photographs and other illustrations are of considerable interest. The author has observed the disease in " one Japanese, several Indians, and approximately three hundred white persons of various nationalities and ancestry, but in no Negroes ". He believes that mepacrine is the principal cause, but is uncertain whether it is the sole aetiological factor ; deficiency of vitamin A may be a predisposing cause. He classifies the eruption as being " dry " or " exudative " ; 80 per cent. of the cases from the South-West Pacific area were of the latter type. Like others, Wilson has noted secondary atrophic changes at the sites of nodular lesions and believes the pigmentation which characterizes the eruption eventually disappears ; he claims to have seen numerous complications " including universal exfoliative dermatitis, hepatitis, atypical pneumonia, polyneuritis, heart bundle-branch block, pericarditis, ascites, a low level of total protein in the blood, reversal of the albumin-globulin ration, edema and anasarca, simple anemia and aplastic anemia. In two patients of this series there developed pulmonary tuberculosis ".

If mepacrine was administered daily in doses of 0·3 or 0·65 gm. to patients exhibiting dry nodular lesions the eruption and the pruritus were aggravated. Not all eczematous eruptions were aggravated when the drug was taken orally. Patch tests with various dilutions of mepacrine appeared to be positive only on those areas where the eruption had been present.

The paper concludes with an interesting comment on the similarity between atypical lichen planus and the toxic manifestations which may occur after the administration of oxophenarsine hydrochloride or solutions of potassium arsenite U.S.P., for both the arsphenamines and mepacrine are said to contain benzyl radicals. *R. M. B. MacKenna.*

PAGE, S. G., Jr. & MCCALL, J. V., Jr. **Delay in diagnosing Malaria after Sulfadiazine Therapy. Two Case Reports.** *Southern Med. J.* 1946, Sept., v. 39, No. 9, 728–31, 2 charts.

Clinical notes of two patients are given. Both had febrile attacks with signs and symptoms indicating pulmonary disease. Both were treated with sulphadiazine. Subsequently, repeated blood examinations failed to reveal the presence of *Plasmodium vivax* which was responsible for the sickness of both patients. The failure to make prompt diagnoses was directly attributable to the administration of sulphadiazine which had freed the peripheral blood of parasites without effecting a cure. *Norman White.*

PERRET-GENTIL, A. Les injections intra-veineuses de calgluquine dans le traitement du paludisme. [**Intravenous Injection of Calgluquine in the Treatment of Malaria.**] *Acta Tropica.* Basle. 1946, v. 3, No. 3, 193–210, 3 figs. [12 refs.]

This preliminary study relates to the treatment of 38 cases of relapsing malaria, mostly *P. vivax* infections, with intravenous injections of Calgluquine. Calgluquine (Sandoz) is a solution 10 cc. of which contains 60 cgm. of quinine gluconate mixed with calcium. The author speaks highly of the results obtained. Thanks to the action of the calcium intravenous injections of Calgluquine are much better supported than intravenous injections of quinine alone. No untoward symptoms ever arose. There was a rapid action on the malaria infection and treatment was followed by considerable improvement in the general condition of the patients. Treatment can be continued over long periods if necessary. Doses of 15 cc. in 24 hours were well tolerated. The injections caused no serious alteration either of blood pressure or of pulse rate. Several patients with experience of many varieties of antimalarial treatment expressed a preference for Calgluquine. *Norman White.*

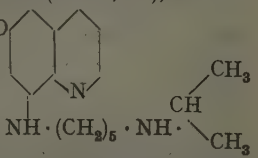
JOHNSTONE, R. D. C. **Relapsing Benign Tertian Malaria treated with 4430.** *Ann. Trop. Med. & Parasit.* 1946, Dec., v. 40, Nos. 3/4, 330–32.

"A six-months' follow-up on 97 patients treated with 4430, compared with a similar number of cases treated with the standard quinine and pamaquin treatment, showed a relapse-rate of over double that of the latter treatment. There is an indication that the interval of time between treatment and further relapse is shorter than in the quinine-pamaquin treatment ; 4430 controls the symptoms of an acute attack of malaria adequately, but cannot be considered of value in the control of relapses."

LOEB, R. F. **Activity of a New Antimalarial Agent, Pentaquine (SN 13,276). Statement approved by the Board for Coordination of Malarial Studies.** *J. Amer. Med. Ass.* 1946, Oct. 12, v. 132, No. 6, 321–3.

This report deals with extensive tests carried out in America on human and bird malaria. with a new synthetic substance, pentaquine (SN 13,276), which is

6-methoxy-8-(5-isopropylaminoamylamino)-quinoline



Tests were also made on its pharmacological and toxic properties in animals and man. The diphosphate of over 95 per cent. purity, which forms yellow

needles and is moderately soluble in water, has been used in these tests. In pharmacological studies on laboratory animals it was found that the drug is rapidly and completely absorbed from the gastrointestinal tract. Only about 10 per cent. of drug administered was recovered in the urine. In plasma, peak values were reached within two hours after administration and the amounts present were negligible after 6 to 8 hours. Estimations were made by coupling with diazotized sulphanilic acid to give a coloured substance. There was no accumulation in tissues after long periods of treatment, the concentrations present being much lower than is found with atebrin or chloroquine [this *Bulletin*, 1946, v. 43, 708] and, in general, the behaviour of the drug resembled that of pamaquin. The findings point to the fact that pentaquine is largely metabolized in the animal body. In man the behaviour of the new drug also resembled that of pamaquin. Great variations in plasma level occurred in persons receiving the same doses. [This fact has also been established for atebrin.]

In acute and chronic toxicity tests, pentaquine was shown to be less toxic than pamaquin ; similar symptoms, such as methaemoglobinemia and stomach cramps, were produced by each. Certain nervous symptoms produced in dogs by pamaquin were not noted after pentaquine, but both drugs affected the heart and circulatory system. In a quantitative sense, quinine increased the toxicity of the drug in rats and monkeys. In man also the toxic effects were similar to those produced by pamaquin, with certain qualitative and quantitative differences depending on the dosage, which in the tests ranged from 15 to 180 mgm. of base per day. Severe anemia was met with in one volunteer.

In infections with *P. gallinaceum* and *P. lophurae*, the drug was respectively 80 and 128 times as active as quinine, and several times more active than pamaquin. Clinical studies were made with the Chesson strain of *P. vivax*, which shows a high relapse rate. In prophylactic experiments in which nonimmune patients were submitted to the bites of infected mosquitoes, pentaquine effected suppression in some cases when a toxic dosage of 120 to 180 mgm. of base was given daily for 8 days. In curative tests, primary attacks in nonimmunes resulting from the bites of 10 infected mosquitoes and also primary and secondary relapses were treated every four hours for 14 days with the result that individual attacks were terminated but relapses were not always prevented even by a high dosage. However, treatment of the third relapse prevented further attacks in 35 patients. Complete eradication was, however, effected in 16 out of 17 cases when the drug was administered daily in 60 mgm. doses combined with 2 gm. quinine, a result which compares favourably with those obtained experimentally when pamaquin is used with quinine. Pentaquine in conjunction with quinine appeared to be less effective when patients were heavily infected through being bitten by 10 infected mosquitoes on three alternate days. The following recommendations are made with regard to dosage :—

" A. *In Suppression and Prophylaxis.*—The toxicity of pentaquine is too great to warrant its use in prophylaxis or prolonged suppression of malaria.

" B. *In Cure of Malaria due to Plasmodium Vivax.*—A daily dose of 60 mg. base (equivalent to 80 mg. of diphosphate) and 2 Gm. of quinine administered concurrently in divided doses every four hours for fourteen days is sufficient to produce radical cure of severe infections due to *P. vivax*. The daily dose of 60 mg. base should not be exceeded. Longer therapy may be necessary when nonimmune persons have been unusually heavily seeded and have not had previous suppressive therapy. Pentaquine (SN 13,276) should be administered only under close medical supervision, preferably during hospitalization. The toxicity of the drug in Negroes and persons of mixed racial extraction and the safe therapeutic dose for children are at present undetermined." *J. D. Fulton.*

FAIRLEY, N. H. **Malaria in the South-West Pacific, with special reference to its Chemotherapeutic Control.** *Med. J. Australia.* 1946, Aug. 3, v. 2, No. 5, 145–62, 10 graphs.

This interesting report deals with the incidence of malaria in the Australian Military Forces in the South-West Pacific during the recent war, the paralysing results of widespread infection during the early stages of the campaign, the formidable obstacles that had to be overcome, and the ultimate triumph, achieved largely by the application of the results of the Cairns experiments, more especially with regard to the efficacy of mepacrine in adequate doses as a suppressant. A large part of this story was revealed by the author in 1945 to the Royal Society of Tropical Medicine and Hygiene (this *Bulletin*, 1945, v. 42, 630).

In 1944–45 malaria had ceased to be an operational problem in all areas but one. The incidence of *P. vivax* malaria, however, among troops returned to Australia for rest and regrouping, following the cessation of mepacrine medication, continued to be very high. The one operational area in which malaria control measures were inadequate was the Aitaipe-Wewak area of New Guinea. Some 27·6 per cent. of the total force engaged in this area developed overt malaria. *P. falciparum* was found in 78 per cent. of these overt cases. There is reason to believe that during the eleven months of exposure to infection in this area not less than 90 per cent. of the force were infected with *P. falciparum* or *P. vivax* or both, so that mepacrine even here was not an ineffective suppressant. Very thorough investigations indicated that the cause of failure in all cases of *P. vivax* malaria and in more than two-thirds of the *P. falciparum* cases was defective mepacrine discipline. About one-third of the overt cases of malignant tertian malaria appeared to have been caused by infection with a relatively mepacrine-resistant strain of *P. falciparum*. In persons infected with this strain 0·1 gm. of mepacrine taken every day is not effective in suppressing malaria; double this dose would generally suppress overt attacks but would not always produce radical cure. This relatively resistant strain is not mepacrine-fast; it seemed that the quality of mepacrine resistance was "in the making" rather than a fixed biological characteristic of a local strain. Sub-optimal dosage may have been responsible for its development. No increased resistance to antimalaria drugs other than mepacrine and santochin was exhibited by this strain. An adequate summary of this important paper is not possible. *Norman White.*

SELBY, C. H. **Malaria in the South-West Pacific: Additional Facts about Malaria Control in the Australian Military Forces.** [Correspondence.] *Med. J. Australia.* 1946, Aug. 24, v. 2, No. 8, 286–7.

The word "additional" in the title of this contribution refers to Brigadier N. H. FAIRLEY's article (see above). The author describes the careful manner in which measures of personal prophylaxis—mosquito nets and repellents—were carried out among the Australian Forces. With reference to the higher incidence of overt malaria in the Aitape-Wewak area than elsewhere during eleven months of 1944–45 the author states that antimalaria discipline was no more lax there than in other operational theatres. In the Bougainville and New Britain areas, which compared so favourably with Wewak, the suppressive dose of mepacrine being taken was in many cases more than the official one tablet a day. Moreover in the Wewak area it was never possible to arrange a DDT spray before, or soon after, the arrival of troops. In some other areas

this was done. Variations in malaria incidence may have been caused by several variable factors and discipline may not have been a factor at all.

Norman White.

FAIRLEY, N. H. *et al.* **Atebrin Susceptibility of the Aitaipe-Wewak Strains of *P. falciparum* and *P. vivax*—a Field and Experimental Investigation by L.H.Q. Medical Research Unit, Cairns.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Dec., v. 40, No. 3, 229–73, 8 charts.

This paper describes in detail the investigations that were carried out with atebrin-resistant strains of *P. falciparum* obtained from soldiers with naturally acquired infections in Aitaipe-Wewak, New Guinea. Nine selected patients were sent by air-ambulance to Cairns, selected for their tendency to recrudesce after standard quinine, atebrin, plasmoquine treatment or for some other reason such as hyperinfection. The strain or strains obtained from seven of these patients were atypical inasmuch as the infections they caused in experimentally infected volunteers taking 0·1 gm. atebrin daily were not suppressed, though the suppressive medication was continued for 28 days after the last exposure to infection. An increase of atebrin to 0·2 gm. a day was not always effective. Four volunteers so infected received the standard course of quinine, atebrin plasmoquine followed by 0·1 gm. atebrin daily : only one of them was radically cured. Paludrine in doses of 0·025 to 0·1 gm. daily acted as a complete causal prophylactic against all strains.

Such atebrin-resistant strains of *P. falciparum* were encountered nowhere else in New Guinea or New Britain and only accounted for a minority of infections in the Aitaipe-Wewak area.

In one case, a strain lost its atebrin-resistance after the fourth passage through mosquitoes. The quality of atebrin-resistance may have arisen suddenly as a mutation in soldiers taking atebrin or may be an inherent biological characteristic of a geographically limited strain. It was first demonstrated in an individual who was avoiding taking atebrin ; it might thus be a result of prolonged suboptimal dosage.

No evidence of atebrin-resistant strains of *P. vivax* was obtained.

Norman White.

KNOWLES, F. L. & SMITH, C. S. **Duration of Toxicity of Several DDT Residual Sprays under Conditions of Malaria-Control Operations.** *Pub. Health Rep.* Wash. 1946, Dec. 13, v. 61, No. 50, 1806–10.

" To determine the duration of toxicity for mosquitoes of several DDT residual sprays, 72 houses were sprayed with 4 formulas of DDT spray at the beginning of the ' malaria season,' on about June 1, and were inspected at 6 different periods until October 1, 1945. Twenty-five unsprayed houses in the same area were inspected at the same time.

" For the period of the ' malaria season,' in this region a period of 17 weeks, the once-sprayed houses harbored significantly fewer mosquitoes than the unsprayed houses.

" Little difference was found in the duration of toxicity of the four formulas of DDT residual spray employed, except for the formula used in the houses in group C, which was statistically less effective 14 weeks after spraying."

SEELER, A. O. & MALANGA, C. **Effect of Boric Acid on Avian Malaria.** *Proc. Soc. Exper. Biol. & Med.* 1946, Oct., v. 63, No. 1, 194–5.

FEDERATION PROC. Baltimore. 1946, Sept., v. 5, No. 3, 390–407. **Symposium on Biochemistry of Malarial Parasites. Introduction** [CLARK, W. M.] p. 390. **Enzyme Systems operating within the Malarial Parasite** [EVANS, E. A., Jr.]. pp. 390–96. [20 refs.] **Chemical and Nutritional Observations on Malarial Parasites grown *in vitro*** [BALL, E. G.]. pp. 397–9, 2 figs. **Metabolism of the Malarial Parasite. Action of Antimalarial Agents upon Separated *Plasmodium lophurae* and upon certain Isolated Enzyme Systems** [HELLERMAN, L., BOVARNICK, Marianna R. & PORTER, C. C.]. pp. 400–405. [20 refs.] **The Influence of Napthoquinones upon the Respiratory and Carbohydrate Metabolism of Malarial Parasites** [WENDEL, W. B.]. pp. 406–7.

The introduction by the Chairman of the Panel on Biochemistry and Member of the Board for Co-ordination of Malarial Studies, National Research Council of America, reviews briefly the researches described below which represent some of the investigations carried out in America under a co-operative scheme during the late war. The immediate object of these studies was to obtain information on the metabolism and essential growth factors of malaria parasites which might be of help in the synthesis of more potent antimalarials. The wider aspect of the biochemistry of these parasites was also considered.

The first paper is an excellent summary by EVANS of the facts known about the enzyme composition of malaria parasites. In the elucidation of these facts, he himself has played an important part. Studies on the biochemistry of these organisms, initiated in Britain, have been continued and developed to a remarkable extent in America by the use of different human, avian and monkey species of parasite.

Because of technical difficulties only the erythrocytic stages of the different parasites have been investigated, either in, or free from, the host red cell or in cell-free extracts. Remarkably similar reactions are brought about by all types which, so far, have failed to provide an explanation of species specificity. Parasites free from red cells lack some of the metabolic activities of parasitized erythrocytes. It appears that heavy metal catalysts of the cytochrome system, flavoproteins, proteinases and certain dehydrogenase systems play a part in parasite metabolism. Synthesis and breakdown of cholesterol and phospholipids also occurs, and haemoglobin is split up. The production of ammonia and amino-nitrogen is apparently associated with oxidation processes. Carbohydrate metabolism has been intensively studied. Many different substrates can be oxidized by the various plasmodial species and a number of oxidation products have been detected. The intermediate steps in the pathway of glucose utilization, which involve phosphorylation, have been determined and appear to resemble similar reactions in other organisms and tissues. Certain differences, such as sensitivity to antimalarials, have nevertheless been noted in the enzyme systems of malaria parasites and their tissue analogues, possibly as a result of differences in enzyme composition. The author believes that " The further study of this fact may prove to be of the greatest importance in understanding the differential effect of chemotherapeutic agents on the parasite and its host."

BALL and his colleagues have elaborated new *in vitro* techniques by which malaria parasites can grow and multiply. Good results were obtained with *P. knowlesi* which increased in numbers from two to elevenfold under experimental conditions within 24 hours. The medium employed contained " a mixture of salts, glucose, amino-acids, vitamins, purines, pyrimidines and several other organic components." Growth and multiplication also occurred to a lesser extent in a medium which contained only glucose and *p*-aminobenzoic acid in salt solution. The acid appears to be an essential growth factor but the

nature of other such factors has not yet been determined. It is probable that others are supplied by serum and red cells present in the more complex medium. Progress in elucidating the nature of such factors has been made by growing parasites in medium containing red cells washed free of serum in presence of a low concentration of crystalline albumin. It has also emerged that low oxygen tensions are necessary for *in vitro* growth, and suggests that the particular habitat of the parasite—the red cell—has not been selected on account of the higher oxygen tension prevailing there. The *in vitro* technique is also of value, in conjunction with that *in vivo*, in studying the action of possible degradation products of the antimalarial agents. Results suggest that the action of quinine and atebrin is due to the unchanged drug. The method has also allowed the demonstration of the antagonism which exists between sulphadiazine and *p*-aminobenzoic acid, on other than first generation of parasites grown *in vitro*. Observations have also been made by both methods on phosphorus exchanges, glucose utilization and other chemical reactions occurring during growth.

Hellerman and his co-workers have investigated the mechanism of action of a number of antimalarials. Their observations were made on erythrocytic forms of *P. lophurae* both in and free from red cells as well as on isolated enzymes. It was found that phosphorylating reactions which occurred during the utilization of glucose by the parasite were interfered with by certain antimalarial agents. Data were also obtained on the combination of specific proteins with agents of this type. The oxidation of a number of substrates by erythrocyte-free parasites was observed. In the absence of added substrate, respiratory activity was negligible but was re-established by adding adenylic acid or adenosine triphosphate, which possibly allowed some intracellular substrate to be used. These parasites, when devoid of all extraneous substrate, showed a marked delay in oxidizing added glucose. The induction period was considerably shortened by fumarate, succinate, adenylic acid or adenosine. The inhibition of respiration by a number of reagents, including those with affinity for sulphydryl groups, is recorded. Adenylic acid or adenosine were able to reverse the inhibitory action of atebrin and certain other compounds on respiration in the case of cells which had been deprived for a time of glucose. Phosphorus exchanges in cell suspensions during incubation were therefore studied. From their action on pancreatic lipase, lactic dehydrogenase and amino-acid oxidase it appeared that atebrin, quinine, sulphonamides and certain other reagents could combine reversibly or irreversibly with proteins. These observations may prove of importance in regard to enzyme activity in general.

Wendel made early and important contributions on the respiratory metabolism of malaria parasites and in this connexion has recently investigated the activity of 3-hydroxy-1,4-naphthoquinone derivatives. It had been noted that these substances were active against *P. lophurae* infections in ducks as well as in *P. knowlesi* infections of monkeys, but were only slightly or not at all active in human malaria infections, and a number of their degradation products were found in the patients' blood. The data suggested that the compounds in question suffered different fates in the various hosts or, in their action, displayed a marked species specificity. The mechanism of their action was therefore studied on *P. knowlesi* and *P. lophurae in vitro*. It was found that 69 out of 76 compounds inhibited parasite respiration to a degree which paralleled their antimalarial activity *in vivo*. The agreement obtained in the two types of experiment depended largely on the nature of the substituent group in position 2 of the molecule. When the drug was active both *in vivo* and *in vitro*, the serum of treated ducks always caused inhibition of respiration *in vitro*. Certain general conclusions were reached from observations on duck red cells parasitized with *P. lophurae* regarding the factors which influence the

action of naphthoquinones. Thus an effect on respiration, reversible in the early stages, is caused by a suitable concentration of those compounds active *in vivo*, this effect being markedly sensitive to *p*H changes and dependent on the concentration of the medium. The inhibition of oxygen uptake results from interference with carbohydrate oxidation, normal duck red cells being influenced qualitatively in the same way as parasitized cells. A method for studying the rate and degree of metabolic degradation of the above mentioned compounds was based on their extraction from the plasma of treated patients followed by comparison of their inhibitory effect on respiration with that of the original drug.

[The researches discussed in the above series of papers have been regularly reviewed in this *Bulletin*. The earliest reference is for the year 1936.]

J. D. Fulton.

GORDON, R. M. & HILL, M. A. **A Technique for obtaining Bacteria-free Suspensions of Sporozoites from the Salivary Glands of Infected Mosquitoes.** *Ann. Trop. Med. & Parasit.* 1946, Apr., v. 40, No. 1, 113–15.

The authors have devised a technique for obtaining suspensions of malarial sporozoites free from bacterial or fungal contamination. The observations were made on *Aëdes aegypti* infected with *P. gallinaceum*. A lightly anaesthetized mosquito is held by the proboscis in forceps in rapidly falling drops of 75 per cent. alcohol for 1½ minutes. It is then drained on two successive slips of sterile filter paper and transferred to a drop of Tyrode's solution on a slide where the salivary glands are dissected under a dissecting microscope without cutting through the oesophagus. The dissected glands are removed to another drop of Tyrode's solution on another slide where they are broken up to liberate the sporozoites. Throughout these operations the strictest aseptic precautions are maintained with sterile instruments and fluids. Sterility is tested by inoculation of Brewer's sodium thioglycollate medium, which is commonly used for testing the sterility of blood plasma, and viability of the sporozoites is proved by inoculation of chicks.

In a table are shown the last series of dissections carried out in 46 mosquitoes. In every case the final suspension contained infective sporozoites and was bacteriologically sterile. It is suggested that these sterile suspensions of sporozoites may be of value in cultivation experiments in tissue cultures in which hitherto sporozoites have failed to develop, possibly because of the presence of penicillin which has been added to counteract the growth of the contaminating bacteria which were always present.

C. M. Wenyon.

TREMBLEY, Helen L. *Aëdes atropalpus* (**Coq.**) **a New Mosquito Vector of** *Plasmodium gallinaceum* **Brumpt.** *J. Parasitology.* 1946, Oct., v. 32, No. 5, 499–501. [11 refs.]

This is a short account of some experimental work on the infection of *Aëdes atropalpus* with *Plasmodium gallinaceum* carried out at the National Institute of Health, Maryland, U.S.A.

The mosquitoes were bred in the laboratory, fed on an infected chick and then kept at temperatures of 28° to 30°C. and 80 per cent. relative humidity. In preliminary studies, 45 out of 53 *A. atropalpus* were found to be infected. Comparison of the incidence of infection in corresponding lots of *A. atropalpus* and *A. aegypti* based on examination of the midguts, salivary glands or both, showed that 90 per cent. (78 out of 87) of the former species and 64 per cent. (56 out of 87) of the latter were positive. Comparison of the intensity of infection based on oöcyst counts, on 37 midguts for each species, showed a greater intensity in *A. atropalpus* ($111{\cdot}94 \pm 23{\cdot}43$) than in *A. aegypti* ($9{\cdot}75 \pm 3{\cdot}98$).

Transmission by *A. atropalpus* was attempted on 26 chicks through three successive generations; three chicks died of undetermined cause and of the remaining 23, 20 developed infection. *H. S. Leeson.*

Roos, A., Hegsted, D. M. & Stare, F. J. **Nutritional Studies with the Duck. IV. The Effect of Vitamin Deficiencies on the Course of *P. lophurae* Infection in the Duck and the Chick.** *J. Nutrition.* 1946, Nov. 11, v. 32, No. 5, 473–84. [10 refs.]

"The effects of nicotinic acid, thiamine, choline, and vitamin A deficiency on the course of P. lophurae infections in chicks and ducklings are reported.

"In chicks, vitamin A deficiency appears to cause a somewhat milder infection and choline deficiency may have the opposite effect. Thiamine deficiency appeared to have no influence on the infection. Nicotinic acid deficiency resulted in a much more severe infection. The percentage of parasitized cells was from four to five times greater in the deficient birds. Both deficient and nondeficient birds were able to clear the blood stream of parasites in approximately the same length of time.

"In ducks none of the deficiencies influenced the course of the infection to a marked degree. The duck is probably too susceptible to this infection to be a satisfactory experimental animal."

Dearborn, E. H. **Filtrable Agents Lethal for Ducks.** *Proc. Soc. Exper. Biol. & Med.* 1946, Oct., v. 63, No. 1, 48–9.

"Filtrable agents, lethal for ducks, were obtained by Seitz filtration of plasma from ducks with lophurae, cathemerium, relictum or elongatum malaria. Attempts to free the malaria of the filtrable agent were unsuccessful."

Dearborn, E. H. & Marshall, E. K., Jr. **Curative Action of Drugs in Lophurae Malaria of the Duck.** *Proc. Soc. Exper. Biol. & Med.* 1946, Oct., v. 63, No. 1, 46–8.

"A number of drugs have been examined for their curative action in lophurae malaria in the duck. Pamaquine appears to cure a fair percentage of the birds, while quinine, quinacrine, chloroquine and a number of other drugs do not."

TRYPANOSOMIASIS.

Fulton, J. D. & Lourie, E. M. **The Immunity of Mice cured of Trypanosome Infections.** *Ann. Trop. Med. & Parasit.* 1946, Apr., v. 40, No. 1, 1–9. [25 refs.]

Ehrlich and Shiga (1904) first demonstrated the fact that mice cured of trypanosome infections were immune to reinfection with the homologous strain. Since that time many studies have been made, chiefly with strains of *T. brucei* and *T. rhodesiense* against infections with which curative drugs have long been known. The recent discovery of compounds with curative action in infections due to *T. congolense*—certain phenanthridinium derivatives and diamidines—have made it possible to carry out similar studies with this trypanosome. Such studies have been carried out by the authors of the paper under review. At the same time they have re-investigated immunity phenomena in mice cured of other infections (*T. rhodesiense* parent strain, atoxyl-fast strain,

suramin or Bayer 205 fast strain, *T. equinum*, *T. equiperdum*). All these strains produce fulminating infections in mice, trypanosomes appearing in the blood in 1–3 days after intraperitoneal inoculation. The immunity was tested by inoculation after cure of the primary infection of trypanosomes of the homologous strains or of trypanosomes of heterologous strains. The results were considered under three headings—no re-infection, re-infection with incubation period at least five days longer than in the controls, re-infection with the same incubation period as in the controls.

Tests of immunity against homologous strains were carried out with the three strains of *T. rhodesiense* and the strain of *T. congolense*. In 128 such tests immunity was absent in only four instances. Complete failure to become re-infected occurred 26 weeks after treatment of a *T. rhodesiense* infection and 20 weeks after treatment of a *T. congolense* infection. LOURIE and O'CONNOR [this *Bulletin*, 1937, v. 34, 123] have already shown for *T. brucei* and *T. rhodesiense* persistence of immunity for eight months and six and a half months respectively, while BROWNING and CALVER [this *Bulletin*, 1945, v. 42, 259] have noted immunity of 13 months' duration for a strain of *T. congolense*. When such immunity breaks down, it may be due to the trypanosome having undergone a change in its antigenic structure during the passages which have occurred between treatment and the immunity tests, or the trypanosomes inoculated at the test may possess the facility of acquiring an anti-serum-fast character. In this conception of the immune state its persistence or not is related to the stability of the antigenic constitution of the trypanosomes rather than to the mouse's power of developing and retaining immunity. In support of this view the results of certain tests of the lytic power of sera are advanced, as also the well-known fact first demonstrated by FRANKE (1905) and EHRLICH (1909) that the trypanosomes of a relapse are immunologically different from those of the first infection. It is this antigenic lability which partly accounts for the difficulty of immunizing men or beasts against trypanosomes in the field where a considerable multiplicity of antigenic types occur.

As judged by immunity tests, *T. congolense* is more antigenically labile than *T. rhodesiense*, a fact which would prevent the host's acquired immunity from completing the eradication of an infection after non-sterilizing courses of treatment. The interesting observation was made that there was no cross-immunity between the strain of *T. rhodesiense* and the strain which had been made suramin-resistant, whereas there was complete cross-immunity between it and the atoxyl-resistant strain. It is pointed out that the resistant strains are essentially relapse strains which are known to differ immunologically from the parent strain and that in the course of subsequent passages in mice they may revert immunologically to the parent type. *C. M. Wenyon.*

ROMAÑA, C., GIL, J. & DE ROMAÑA, M. S. Indices de infección de niños por *S. cruzi* en escuelas de Tucumán, Santiago del Estero y Catamarca. [**Incidence of Infection by *T. cruzi* in School-Children in Tucumán, Santiago del Estero and Catamarca.**] *An. Inst. Med. Regional.* Tucumán, Argentine. 1946, Aug., v. 1, No. 3, 317–32, 9 figs. & 1 map. English summary.

Xenodiagnostic and complement fixation tests were carried out on a number of children of the schools of the places mentioned. For xenodiagnosis the authors used nymphs of *T. infestans*, *T. rubrovaria*, *T. sordida*, *T. platensis* and *Panstrongylus megistus*.

In two schools in Trancas (Tucumán) 48 children were examined, 28 boys and 20 girls, between 5 and 15 years of age. Twelve were positive to xenodiagnosis; the sera of 10 were tested for complement fixation and 8 were positive (3 or 4 plus). Next month, 30 children at Tapso, on the border between

Catamarca and Santiago del Estero, and 20 in a school at Achalco, 5 kilometres distant, in Catamarca Province were tested. Xenodiagnosis proved positive in 5 of the former and 3 of the latter, or in 8 of the 50. By complement fixation the proportion of positive results was much higher, being 24 out of the 50. One child, a girl of 11 years, had frequent extrasystoles ; she had proved negative to the xenodiagnostic test but gave a 3 plus to complement fixation. Among 25 children examined at Rio Hondo, Santiago del Estero, 9 were xenodiagnostically positive and all gave positive complement fixation reactions, as did also one who had been negative to xenodiagnosis. Lastly, 23 schoolchildren in the town of Catamarca were examined by xenodiagnosis and 5 were positive.

Altogether, therefore, 146 were tested by xenodiagnosis and 34, or 23·3 per cent., were positive. Of 82 sera tested for c.f., 42 (51 per cent.) gave 3 or 4 plus. [None of the figures given in the authors' summary are correct, according to the text numbers.] *H. Harold Scott.*

Romaña, C. & Gil, J. Reacción de fijación de complemento con antigeno de cultura de *S. cruzi* en 500 sueros humanos. [**Complement Fixation in Chagas's Disease, with a Culture of *T. cruzi* as Antigen.**] *An. Inst. Med. Regional.* Tucumán, Argentine. 1946, Aug., v. 1, No. 3, 297–304. English summary.

Various antigens obtained from cultures of the trypanosomes have been used for this reaction from time to time ; in 1936 Kelser's, in 1942 the Romaña-Dias alcoholic antigen, in 1943 Davies's water culture and, lastly, the purest of all, the polysaccharide antigen of Muniz and Freitas. The present author used the Romaña-Dias antigen for 200 sera ; the results were fairly satisfactory, but a large amount of culture was required.

For the study recorded in this paper the culture was obtained from a strain from *T. rubrovaria* which had proved very active in infecting laboratory animals. The culture medium was composed of : Meat extract 5 gm., NaCl 5 gm., agar 12 gm., water 1,000 cc., adjusted to *p*H 7·4–7·6. After sterilization and cooling to 55°C., defibrinated sheep's blood is added to 10 per cent., and on solidification the surface is covered with glucose broth. On this a rich culture was obtained in 10–15 days. For preparing the antigen the liquid part of the medium is withdrawn, centrifuged and washed three times with physiological saline ; the deposit is separated and to it is added 10 times its volume of saline with phenol to 0·5 per cent., mixed with powdered glass, the whole being vigorously shaken to break up the trypanosomes. The suspension, decanted from the powdered glass, forms the stock which is put up in ampoules and diluted for use in the test. This antigen retained its potency unchanged for 7 months, but began to lose it after that time. Later, the author used merthiolate, 1 : 10,000 physiological saline, as a preservative. The results of the test with 500 sera may be summarized as follows : Of 15 in whose blood *T. cruzi* was seen, 14 gave a positive (4 or 3 plus) and one a negative (1 or 2 plus was regarded as negative) ; the negative was from a child in a very early stage, about the fourth day, of disease. Chagas himself used to say that a positive ought not to be expected for a month. Of 63 positive by xenodiagnosis 61 were positive by the c.f. test. This occasional negative in patients xenodiagnostically positive has been noted before ; it may be due to transient diminution of antibody in the blood, for the same case examined on another day may be positive. Among 341 suspicious cases—suspected on account of cardiac or nervous signs or symptoms—149 were positive, 192 were negative ; of 31 syphilitic sera 12 were positive to Chagas's antigen test. All gave a positive Wassermann, but in 12 the Chagas's c.f. test remained positive after the syphilis had been treated and the W.R. had become negative.

Among 15 patients suffering from cutaneous leishmaniasis, five were negative, 10 were positive, but not strongly. This disease—the fact has been noted by others also—gives a weak positive to tests for Chagas's disease. Of three suffering from brucellosis, two were negative, one positive, but the last came from a district heavily infested with Triatomidae. Thirty-two cases were from normal subjects or those suffering from disease other than Chagas's disease and all were negative.

The test is, therefore, of much value. In the authors' words :—" The specificity of the reaction is verified. . . . The reactions are positive only in cases of Chagas's disease or [weakly] in cutaneous leishmaniasis." [A paper of much interest.] *H. Harold Scott.*

LEWIS, Mary N. **Exudative Trypanosome Pleuritis of Mice infected experimentally with** *Trypanosoma cruzi. Proc. Soc. Exper. Biol. & Med.* 1946, Oct., v. 63, No. 1, 30–31, 1 fig.

" In the course of the infection of young mice with *T. cruzi* the incidence of pleuritis was observed in 3·6 to 50 per cent. of the cases depending on the size of the inoculum. The serous exudate which was sterile if examined with bacteriological methods contained numerous trypanosome forms and intracellular leishmania-like bodies."

KLYUEVA, N. G. & ROSKIN, G. **Cancerolytic Substance of** *Schizotrypanum cruzi Amer. Rev. Soviet Med.* 1946, Dec., v. 4, No 2, 127–9.

FINDLAY, G. M., HARDWICKE, J. & PHELPS, A. J. **Tsetse Fly Repellents.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Dec., v. 40, No. 3, 341–4.

" Under field conditions nine compounds were tested for repellent action against tsetses. Indalone, Formula 622, *N-n*-amylsuccinimide, 2-phenylcyclohexanol and *n*-butyl-*dl* malate possessed some activity."

LEISHMANIASIS.

HENTZ, H. & NOEL, G. Le premier cas de kala-azar en Belgique. **[The First Case of Kala Azar in Belgium.]** *Rev. Belge Sci. Méd.* 1942, Dec., v. 14, No. 10, 403–7. [13 refs.]

ADLER, S. & TCHERNOMORETZ, I. **Failure to cure Natural Canine Visceral Leishmaniasis.** *Ann. Trop. Med. & Parasit.* 1946, Dec., v. 40, Nos. 3/4, 320–24, 3 figs. on 1 pl.

" In the laboratory we have failed to cure dogs naturally infected with *L. infantum* by treatment with 4 : 4′-diamidino stilbene.

" In the field we have observed failure to cure infected animals by intensive treatment with neostibosan.

" After intensive treatment there is a residual infection in the corneo-sclerotic junction, lymphatic glands and skin. The latter serves as a source of infection for sandflies and, through them, for other dogs and man.

" Pending a further advance in the chemotherapy of visceral leishmaniasis, infected dogs should be either removed from endemic centres or destroyed.

" It is interesting to note that infected bitches produced healthy litters."

FEVERS OF THE TYPHUS GROUP.

BENDICH, A. & CHARGAFF, E. **The Isolation and Characterization of Two Antigenic Fractions of *Proteus* OX-19.** *J. Biol. Chem.* 1946, Nov., v. 166, No. 1, 283–312. [65 refs.]

The properties of antigenic fractions isolated from *Proteus OX19*, the organism agglutinated by sera of patients suffering from louse-borne typhus (Weil-Felix reaction), have been examined. The extraction of the organisms with trichloroacetic acid or, less effectively, their digestion with crystalline trypsin affords two homogeneous antigenic fractions differing in immunological specificity and particle size. The heavy fraction (C-2), sedimentable at high centrifuge speeds, shows specificity towards typhus sera as well as to *Proteus* antisera, the lighter fraction (C-11) shows only *Proteus* specificity. The typhus specificity of C-2 is lost when the fraction is heated or freed from lipins.

Both antigens are complexes consisting of : (*a*) lipins (with a high proportion of free fatty acids) ; (*b*) a protein (containing arginine, lysine, glutamic acid, leucine, *iso*leucine, proline, and phenyl alanine, but not histidine, tyrosine or tryptophan) ; (*c*) a polysaccharide (containing N-acetylglucosamine, mannose, galactose, and perhaps glucose). Part of the organically bound phosphorus is present in the form of an extremely acid-labile linkage. *J. H. Birkinshaw.*

MALCOMSON, M. Elizabeth & WISHART, F. O. **Studies of the Serology of Typhus Fever.** *Canadian J. Pub. Health.* 1946, Oct., v. 37, No. 10, 411–21. [11 refs.]

The authors describe the results obtained in a study of the complement-fixation responses observed in guineapigs and human beings after vaccination and infection with murine- and epidemic-typhus rickettsiae.

When type-specific antigens were used, vaccinated guineapigs reacted against the homologous antigen at titres more than four times higher than against the heterologous antigen, but the responses were so irregular that the reaction was not considered suitable for testing the potency of vaccines.

Among 81 persons immunized by a combined epidemic and murine vaccine (two parts epidemic to one part murine) nearly all gave a higher-titre response against epidemic than against murine antigen. Five months later the titres had fallen greatly, sometimes almost to zero, but after a recall dose of vaccine they rose to a greater height, and were more persistent, than they had been after primary vaccination.

Sera of 50 typhus patients treated in the Middle East were received from Major van Rooyen ; when these were tested against soluble antigens, high titres (1–800 or over) were observed in most of the cases ; but in 21 the epidemic and murine titres were the same, and in 25 there was only a two-fold difference in the titre, so that differentiation between the two types of the disease was rarely possible.

When a common (heat-stable) antigen was used comparable results were obtained ; but with a type-specific antigen differentiation of the type was usually possible, in 60 per cent. the epidemic titre was at least four times higher than the murine, in 8 per cent. it was twice as high, and in the remaining cases the sera were anticomplementary or otherwise unsatisfactory, probably owing to prolonged storage.

In 22 cases of suspicious illness among laboratory workers who had been protected by a bivalent vaccine the disease was shown to be typhus by the occurrence of a rising-titre complement-fixation reaction. Using type-specific antigens 14 of the cases could be classed as epidemic on the strength of an

epidemic titre four times higher than the murine, and correspondingly 3 could be classed as murine; in the remaining 5 cases there was only a two-fold difference in the titre; in most of the 22 cases the higher titre was 1–800 or over.

The explanation of the concurrent rise in the two types of antibodies is not known.

The authors conclude that when common and type-specific antigens are used the complement-fixation reaction is the test of choice in cases in which tests involving the use of infective rickettsiae cannot be carried out.

[The question of the reliability of the complement-fixation test as a method of differentiating between epidemic and murine typhus seems to be still *sub judice*.] *John W. D. Megaw.*

MALCOMSON, M. Elizabeth & WISHART, F. O. **Studies of the Serology of Typhus Fever.** *Canadian J. Pub. Health.* 1946, Nov., v. 37, No. 11, 461–6. [18 refs.]

The chief conclusions stated in this paper are :—(1) The Weil-Felix test is of little value as a method of testing antibody response to vaccination against typhus. The reaction is positive in 50–75 per cent. of vaccinated persons, and rarely at a high titre. (2) Equally poor results are obtained by complement-fixation tests in which the heat-stable antigen, common to that of *Proteus OX19*, is employed. (3) In typhus fever among vaccinated persons there is no significant rising-titre response to the Weil-Felix test. (4) When *Pr. OX19* antigens are used in complement-fixation tests, the results are comparable with those obtained with the Weil-Felix tests in vaccinated persons and also in typhus patients who had not been vaccinated. (5) The Weil-Felix reaction becomes positive earlier than any other serological test for typhus fever, but it suffers from the drawback of incomplete specificity, whereas the rickettsial complement-fixation reaction, when type-specific antigens are used, can differentiate between murine and epidemic typhus.

The authors used living suspensions of non-motile colonies of *Pr. OX19* in carrying out the Weil-Felix test; these were found more sensitive than any of the killed suspensions.

Details of the experiments on which these conclusions are based will be found in the paper. *John W. D. Megaw.*

GILLIAM, A. G. **Efficacy of Cox-Type Vaccine in the Prevention of naturally acquired Louse-borne Typhus Fever.** *Amer. J. Hyg.* 1946, Nov., v. 44, No. 3, 401–10.

The author gives a detailed account of a critical study of the efficacy of an ether-extracted yolk-sac vaccine manufactured in 1942, and administered to 743 employees of the Cairo Fever Hospital between February and June 1943; 136 other employees received no vaccine. Among the vaccinated persons 111 received only one dose; 138 received two doses; and 494 received the full course of three doses. Persons who were attacked by typhus fever less than four weeks after receiving the vaccine were regarded as not having been effectively immunized.

Altogether 48 attacks occurred, and when allowance was made for the various disturbing factors it was estimated that one or two doses of the vaccine " were somewhat effective in ameliorating the clinical course" of the attacks, but had little effect in protecting against the occurrence of attacks, whereas the full course of three doses reduced the attack rate to a degree which was of borderline statistical significance.

The results were as shown in the table :—

Effective vaccinal state	No vaccine	One dose	Two doses	Three doses
Number of attacks	28	6	10	4
Attack rate per 10,000 person weeks	27·8	35·8	72·9	16·4

The author mentions that later work has resulted in the preparation of a more potent vaccine, which is now given as two primary doses followed later by " booster " doses at intervals.

[The paper is a model of careful observation and of scientific caution in the interpretation of the findings.] *John W. D. Megaw.*

Fajerstein, S. G. & Besdenjesznich, K. V. [**The Efficacy of Vaccination and Revaccination against Typhus.**] *Hygiène et Service Sanitaire.* Moscow. 1946, No. 6, 43–8. [In Russian.]

During the years 1942–1944 anti-typhus vaccinations were carried out amongst the staff of 12 Moscow railway stations. Persons vaccinated were those considered to be exposed to infection by virtue of close contact with passengers and included station workers, station police and NKVD, train crews, and medical staff. Three injections of 0·5–1–1 cc. were given, with intervals of 5 to 12 days ; the vaccine of Duren, Krontovskaya and Maevsky was used. A total of 16,797 persons received one course of vaccination, and 6,497 were revaccinated, in successive years. A group of 17,735 was left unvaccinated for control purposes. Local reactions were seen in 5·1 per cent. and general reaction in 7·7 per cent.

Over a one-year period of observation, the morbidity amongst vaccinated subjects was 13·7 per 10,000, and amongst controls 27 per 10,000. In persons revaccinated the incidence was 6·5 (controls 22·6) ; no cases occurred in 1,912 persons revaccinated twice. The disease occurred on an average 3·7 months after the completion of the first vaccination, and 4·5 months after revaccination ; the course was considerably milder than in control subjects. *D. J. Bauer.*

Cowper, S. G. **A Note on a Disinfestation Plant used in a Typhus Hospital for Prisoners of War in Germany.** *J. Roy. Army Med. Corps.* 1946, Oct., v. 87, No. 4, 173–6, 1 fig.

In this paper, which is illustrated by a sketch plan, the author gives a detailed description of one of the numerous similar disinfestation stations established in hospitals of prisoner-of-war camps in Germany. The author's experience of the station was obtained in the period 1941–1943.

Among 1,904 patients disinfested on arrival at the hospital only four were later found infested with lice ; this result is not surprising in view of the elaborate process of disinfestation to which each patient was subjected before admission to the ward. The protection of members of the staff employed at the station was equally thorough.

The station had nine separate rooms, apart from passages and a detached laundry. The building and equipment were specially planned and constructed, regardless of cost, for the disinfestation and disinfection of the skin and clothing of the patients. Obviously the threat of a widespread epidemic of typhus in Germany was taken very seriously.

Now that DDT and other effective disinfestants are available it is unlikely that the construction of costly static stations of the kind will be contemplated

in the future ; the staff employed at the station could probably maintain a high degree of louse control among the staff and inmates of an entire camp at a lower cost by the simple process of dusting with DDT powder. Experience in Naples, Belsen and other places suggests that disinfestation by itself is sufficient to control epidemics of typhus, though it would doubtless be desirable in addition to employ disinfection for infected persons and their clothing.

John D. W. Megaw.

MELENEY, H. E. & FRENCH, R. S. **Endemic Typhus Fever in Southern California.** Reprinted from *California & Western Med.* 1945, Mar., v. 62, No. 3, 14 pp., 1 chart. [14 refs.]

This paper deals with the reported occurrence of typhus fever of the " endemic " type in California during the period 1922–1942.

Among the 215 cases notified, 152 were from Los Angeles County and 45 from San Diego County ; both of these counties are in the southern part of the State. The disease was predominantly urban, 125 of the cases being from Los Angeles City and 17 from San Diego City.

The months of chief prevalence, in descending order, were :—October (43 cases) ; November (31 cases) ; December (24 cases) ; September (21 cases) ; May (19 cases) ; July (18 cases) ; and August (17 cases). In the remaining months the number of cases ranged from 6 to 10.

In 1925, the disease suddenly ceased to occur in Los Angeles City, presumably because of a campaign of rat control carried out to check an epidemic of pneumonic plague.

Only 0·5 per cent. of the cases occurred among children of the 0–9 age group ; 73 per cent. of the patients were males. Only one case was diagnosed by guineapig inoculation. There were 7 deaths (3·2 per cent.) and only one of these occurred among persons under 40 years of age.

The authors think that the disease may be extending further northwards, and also may be increasing in rural areas. *John W. D. Megaw.*

LEWTHWAITE, R., O'CONNOR, J. L. & WILLIAMS, S. E. **The Tsutsugamushi Disease : Attempted Preparation of a Prophylactic Vaccine from Fertile Hens' Eggs experimentally infected with the Virus.** *Med. J. Australia.* 1946, July 13, v. 2, No. 2, 37–43, 3 figs. [10 refs.]

The investigation described in this paper was carried out in 1942 and 1943 ; it was reported confidentially in the same years but publication was delayed for security reasons. The findings are, therefore, largely of historical interest, though some of them can still be studied with profit by workers on the rickettsia of tsutsugamushi disease.

Several strains of *Rickettsia tsutsugamushi* were cultivated in yolk sacs in the usual way. Eggs were most suitably inoculated after 7–9 days' incubation, and the best yields were obtained from eggs incubated at 35°C. for 7–9 days after inoculation, or till the day of death of the embryo.

Yolk-sac cultures were tested by making smear preparations, which were fixed by methyl alcohol, stained with Jenner-Giemsa stain, and differentiated by acetone. The number of rickettsiae seen in each field ranged from 0 to 200, but the number seen in random-sample counts gave no reliable indication of the antigenic potency of the cultures as judged by their lethal effect on mice.

Yolk-sac suspension did not contain a toxin of the type found in corresponding suspensions of *R. prowazeki*. After successive yolk-sac passages the virulence to mice of a strain was found to have become greatly reduced, though the survival period of inoculated chick embryos remained the same—usually 7–9 days.

Various attempts to obtain richer growths and more concentrated suspensions of the organism were unsuccessful; so also were attempts to immunize mice and guineapigs by a yolk-sac vaccine.

The authors failed to prepare from yolk-sac suspensions antigens suitable for complement-fixation and rickettsia-agglutination tests.

John W. D. Megaw.

HUEBNER, R. J., STAMPS, Peggy & ARMSTRONG, C. **Rickettsialpox—a newly recognized Rickettsial Disease. I. Isolation of the Etiological Agent.** *Pub. Health Rep.* Wash. 1946, Nov. 8, v. 61, No. 45, 1605–14.

The authors report the isolation of a specific rickettsia from a patient suffering from a new disease for which they propose the name rickettsialpox. The disease is said to be the same as the one described by SUSSMAN in an article (*New York Medicine,* 1946, v. 2, 27) dated August 1946, under the title "Kew Gardens Spotted Fever." [The Kew Gardens referred to is presumably in New York.] In October 1946, SHANKMAN reported an outbreak of a similar fever, described as an "Endemic Febrile Illness not yet identified, occurring in New York City" (*New York State J. Med.*, 1946, v. 46, 2156).

The present report is based on a study of an outbreak in which 80 cases occurred during a period of 10 weeks "in a housing development in New York." The only reference to the clinical features of the disease is in the statement that it resembles chickenpox.

In the course of animal-inoculation experiments carried out on 15 patients, a rickettsial organism was isolated from a mouse inoculated intraperitoneally with blood taken from a patient on the 2nd day of his illness. The spleen of the mouse was found enlarged to 8–10 times the normal size, the liver was large and oedematous, and there was a blood-tinged peritoneal exudate. Four serial passages were made through mice, guineapigs, and yolk sacs of embryo chicks. Numerous rickettsia-like organisms were found in yolk-sac smears.

Antigens prepared in three different ways from yolk-sac cultures were used in a large number of complement-fixation tests, in which sera of patients reacted at titres ranging from 1–16 to 1–640; nearly all the sera of Rocky Mountain spotted fever patients also reacted, at somewhat lower titres ranging from 1–8 to 1–512. Sera of healthy persons and of patients suffering from endemic typhus, Q fever and syphilis, gave negative reactions.

Sera of 19 rickettsialpox patients were tested against Rocky Mountain spotted fever antigens; 15 gave positive reactions at titres ranging from 1–4 to 1–320.

Weil-Felix tests (*Proteus OX19*) of an unstated number of rickettsialpox sera yielded only two positive reactions, at titres of 1–100 and 1–200 respectively. Agglutination tests for tularaemia, brucellosis, leptospirosis, and typhoid-group fevers were uniformly negative.

In guineapigs the organisms were readily maintained by intraperitoneal inoculation with tunica scrapings; there was a pronounced scrotal reaction.

Preliminary tests indicated a partial degree of cross immunity with the rickettsia of Rocky Mountain spotted fever. *John W. D. Megaw.*

HUEBNER, R. J., JELLISON, W. L. & POMERANTZ, C. **Rickettsialpox—a newly recognized Rickettsial Disease. IV. Isolation of a Rickettsia apparently identical with the Causative Agent of Rickettsialpox from** *Allodermanyssus sanguineus,* **a Rodent Mite.** *Pub. Health Rep.* Wash. 1946, Nov. 22, v. 61, No. 47, 1677–82.

Two strains of a rickettsia, for which the name *Rickettsia akari* is proposed, have been isolated from pools of mites (*Allodermanyssus sanguineus*) collected

in the development area referred to in the preceding abstract. Some of the mites were collected from house mice (*Mus musculus*), large numbers were found on the outer surface of walls of incinerators.

One of the authors (W. L. J.) was attacked by rickettsialpox three weeks after collecting and processing mites ; he was not aware of having been bitten until he observed an initial lesion seven days before the onset of the fever.

Mites that were not already engorged were allowed to feed on guineapigs or very young mice ; four days later the mites were divided into pools from which suspensions were made and injected intraperitoneally into Swiss mice and male guineapigs. Both strains were found identical in all respects with the strain described in the preceding abstract.

One of the strains was isolated from the brain of a four-day-old mouse on which mites had been fed 10 days previously.

Four additional strains were isolated from pools of mites, but attempts at yolk-sac cultivation were unsuccessful ; two of these strains were from pools of mites already engorged with blood and therefore not allowed to feed again till they were used to inoculate guineapigs.

The only sign of disease observed among the guineapigs used for feeding mites was a vesiculo-papular lesion on one animal at the site where a mite had fed eight days earlier. *John W. D. Megaw.*

ANIGSTEIN, L. & WHITNEY, Dorothy M. **Anti-Rickettsial Activity of Para-Amino-Benzoic Acid (PABA). Evaluation and Significance of PABA Blood Levels in Guinea Pigs with reference to Spotted Fever Treatment.** *Texas Reports on Biol. & Med.* 1946, v. 4, No. 3, 338–52, 2 figs. [11 refs.]

ANIGSTEIN and BADER have already shown that 80 per cent. of guineapigs inoculated with a lethal dose of rickettsiae of Rocky mountain spotted fever recover when para-aminobenzoic acid (PABA) is added to their diet to the extent of 2 per cent. from the time of inoculation. [See this *Bulletin*, 1945, v. 42, 888.]

The present paper contains an account of the results obtained from the administration of PABA in various ways. Parenteral injections of the sodium salt were found unsatisfactory, although high blood-concentration levels of the drug were observed for brief periods after each injection.

Administration by forced feeding was also less satisfactory than mixing the drug with the food. The results obtained by the latter method were as follows:—

(1) Normal diet with PABA (total intake 0·9 to 1·7 gm. per 100 gm. body weight), together with 5 gm. vitamin-free casein daily, failed to save any of six guineapigs, though only one of them became typically ill.

(2) When the casein was replaced by 2 per cent. calcium gluconate the recoveries were 50 per cent.

(3) When the daily diet contained 2 gm. PABA ; 2 gm. calcium gluconate ; and 10 gm. soya-bean flour there was only one death among six treated guineapigs.

The soya bean and casein were given to counteract a fall in the plasma proteins such as is known to occur in human patients suffering from the disease. Calcium gluconate was given to control hypocalcaemia, which is regarded by some observers as an important adverse factor in typhus infection. No mention is made of control guineapigs having been treated by calcium gluconate and a diet containing soya bean without the addition of PABA.

The method of estimating the PABA level of the blood is described, but it is disconcerting to be told that in healthy and infected guineapigs, not treated by any drug, an unknown substance giving the same colour reaction as PBAA

occurs in the blood, soon after a meal, but not in the fasting animals. The presence of this substance in normal conditions "deserves attention in evaluating PABA levels."

The action of PABA is believed by the authors to be "indirect, through a complex mechanism in which the enzyme system of the host and the metabolic requirements of the parasite are involved." *John W. D. Megaw.*

FLINN, L. B., HOWARD, J. W., TODD, C. W. & SCOTT, E. G. **Para-Aminobenzoic Acid Treatment of Rocky Mountain Spotted Fever.** *J. Amer. Med. Ass.* 1946, Dec. 14, v. 132, No. 15, 911–15, 5 charts. [Refs. in footnotes.]

The authors describe the results obtained by the use of *para*-aminobenzoic acid (PABA) in the treatment of 10 cases of Rocky Mountain spotted fever in Wilmington, Delaware, in 1946. The controls available were 21 patients seen in the same area during the period 1938–1946.

Among the treated patients there was only one death, which occurred in a man aged 67 years who was admitted on the 8th day of the illness and who was found at autopsy to have suffered from long-standing renal and myocardial disease. Among the control patients there were five deaths, at the ages of 3, 33, 48, 52 and 63 years.

Dealing only with the 9 treated patients aged less than 40 years, all of whom survived, and the 13 surviving control patients of the under-40 age group, it appears that the average number of days of fever among the former was 10·5, and among the latter 17·5. The temperature of the treated patients dropped rapidly to normal within two to four days of the commencement of treatment, and a decided clinical improvement was observed even earlier.

Composite curves showing the average course of the fever in the above two groups suggest that there was a striking response to treatment.

PABA is rapidly excreted in the urine so that frequent administration is needed to maintain a satisfactory level of blood concentration of the drug; the method found most satisfactory was to give four to six 0·5 gm. tablets every two hours. The total dosage ranged from 50·4 to 327 gm.

The urinary output was found to have an important influence on the blood level of the drug; in one patient the level was 46–48 mgm. per 100 cc. with a daily dosage of 12 gm. and a daily urinary output of 250–500 cc., but when the urine output rose to about 1,500 cc. the level fell below 10 mgm. even with a higher dosage of 20 gm.

The diagnosis was regarded as being certain in every case; it was based on: tick bite or exposure to risk of bite in an affected area; a rising titre agglutination of *Proteus OX19*; and a typical rash, first on the wrists and ankles, then on the palms and soles, and later extending to the trunk.

The results appear to have been surprisingly good, considering that the treatment was started on the average 7·6 days after the onset of the fever.

The maximum PABA blood levels observed during the investigation ranged from 6·5 to 48 mgm. per 100 cc. in the patients who recovered; the optimum level, as suggested by the authors, is 30–60 mgm. The method of estimating the blood level was that described by ECKERT [*J. Biol. Chem.*, 1943, v. 148, 197]. *John W. D. Megaw.*

GALLENSON, N. **Hypertonic Sodium Chloride Solution as Serum Diluent in Agglutination Tests with** *Rickettsia burneti*. *Proc. Soc. Exper. Biol. & Med.* 1946, Oct., v. 63, No. 1, 169–71.

"The use of a 5·0 per cent. solution of sodium chloride as a serum diluent in agglutination tests with *Rickettsia burneti* reduced or eliminated the prozone effect and permitted the employment of a more dilute antigen."

VAN DEN ENDE, M., STUART-HARRIS, C. H., FULTON, F. & NIVEN, J. S. F. **Chemotherapeutic and other Studies of Typhus.**

This book is reviewed on p. 472.

YELLOW FEVER.

TAYLOR, R. M. ; DA CUNHA, J. F. ; LAEMMERT, H. W., Jr. ; FERREIRA, L. de C. **An Epidemiological Study of Jungle Yellow Fever in an Endemic Area in Brazil. Part I. Epidemiology of Human Infections** [TAYLOR & DA CUNHA]. **Part II. Investigations of Vertebrate Hosts and Arthropod Vectors** [LAEMMERT, FERREIRA & TAYLOR]. *Suppl. to Amer. J. Trop. Med.* 1946, Nov., v. 26, No. 6, 69 pp., 5 maps & 3 figs. [79 refs.]

The first part of this important monograph deals with the epidemiology of the disease based on studies made in the vicinity of Ilhéus—a town on the Atlantic seaboard of the State of Bahia, where rural yellow fever, in the absence of *Aëdes aegypti* has been recognized at intervals since 1936, when this mosquito was finally eradicated from the entire region. Viscerotomy posts were established in 1931, and the first positive liver in 1934 came from a three-year-old child, who had lived in a densely wooded locality, in the district of Japu, Ilhéus. This was the first proved case of jungle yellow fever in this region. Four out of the seven remaining members of this family were found to be immune against yellow fever, one a boy seven years old. Subsequently other positive liver specimens were obtained in 1935, 1936, 1940, 1941, 1942 and 1943, in widely separated rural areas, and out of a total of 311 blood specimens from persons in the neighbourhood, 37·3 per cent. gave positive protection tests against yellow fever.

The climate and general features of this region are described in detail and then the scope of the study, which included not only the direct method of trying to isolate the virus and to trace its passage in man and animals, but also the indirect method of determining the habits and environment favouring human infections, and the flora and fauna conducive to the maintenance of virus in the forest.

An immunity survey of the human population was undertaken, by means of neutralization tests, as recommended by THEILER [this *Bulletin*, 1933, v. 30, 714] ; the complement-fixation test was also done.

The percentage of positives was found to be greater in the southern districts of Ilhéus, where it exceeded 30 per cent. These districts contain or border upon the more extensive forests. The relation of occupation to yellow fever immunity in a group of 707 persons shows that the highest percentage of immunes (40·7) occurred among the labourers on cacao plantations, workers on mandioca farms showing 19·5, and children (of no occupation) 11·6 per cent. respectively. The relation of visits to old type forests, aged 75 years or more, to yellow fever immunity is then given in tabular form and the results indicate a correlation between the percentage of immunes and the frequency of visits to such forests.

Thus out of 77 persons making daily visits, 58·4 per cent. were positive, as compared with only 11·9 per cent. in those never visiting the forests. Visits to young type forests (under 75 years of age) did not seem to enhance the chance of acquiring immunity. In all these groups males showed a considerably higher percentage of immunes than females. The immunity rate was also found to be significantly higher in those living in the vicinity of old-type forests.

Fifteen months after the first survey was made, blood specimens of 234 persons who had given negative results were re-examined. Only one, an adult male, was positive on this second survey.

The general results confirm earlier observations that contact with forest is the salient feature associated with infection, and that it is an occupational disease only in so far as the occupation leads to forest contact.

The second part, dealing with the studies on mammals, birds and arthropods, opens with a review of previous work on the subject, followed by a description of the field and laboratory methods employed in the authors' investigations.

A total of 5,322 mammals was collected including Rodentia 2,300, Primates 1,851, Marsupialia 1,040, Chiroptera 81, Carnivora 28, Edentata 21, and one Artiodactyle. These are classified according to order, genus and species, and the type of vegetation where they were captured. The two principal breeding seasons were found to be January to May and August to November; no pregnant females and few young were caught in June, July and December.

Neutralization tests were carried out on a large number of the mammals and a high percentage of sera from certain species of rodents, especially *Oryzomys* spp., neutralized yellow fever virus, but it is believed that this neutralization was the result of some non-specific virucidal substance in the blood rather than to specific immunity to yellow fever virus. Sera from a total of 1,756 mammals and 141 birds were inoculated into non-immune marmosets, many of the sera being pooled before inoculation. All the results were uniformly negative, with the exception of blood from marmosets. On four separate occasions yellow fever virus was isolated from wild *Callithrix penicillata*, during what seemed to be a transient epizootic among these animals. At the same time, and in the same locality, the virus was also obtained from the mosquito *Haemagogus spegazzinii*.

Except for this, a total of 172,873 mosquitoes and also various ectoparasites from rodents and marsupials were tested for virus with negative results.

The highest percentage of immunes was found among marmosets captured in the old-type forests, and in these regions *Haemagogus* mosquitoes were four times more numerous than in other types of forest. There is thus an association of immunity both in humans and marmosets and the prevalence of *Haemagogus* with the older climax type of tropical rain forest.

Although *Metachirus nudicaudatus* and at least one species of *Marmosa* (*M. cinerea*) were susceptible to infection with the yellow fever strain isolated from the marmosets, neutralization tests on the sera of captured marsupials did not suggest that they were involved in the cyclic passage of the strain in nature.

The maintenance of the virus in the region studied may be explained by the Primate-mosquito cycle, involving marmosets and *Haemagogus*. *E. Hindle.*

BATES, M. & ROCA-GARCÌA, M. **The Development of the Virus of Yellow Fever in Haemagogus Mosquitoes.** *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 585–605, 3 figs. [15 refs.]

The authors have recently described the establishment of laboratory cycles of yellow fever virus using haemagogus mosquitoes and Saimiri and douroucouli monkeys caught in the Villavicencio region of Colombia [this *Bulletin*, 1946, v. 43, 32]. They have been studying in detail the principal factors governing mosquito infection with virus and the present paper deals with the effect of variation of the dose of ingested virus and the environmental temperature.

Quantitative estimations of virus have been made by subcutaneous inoculation of 3-day-old mice, as this method gave results almost identical with that of intracerebral inoculation of 7-day-old mice and produced fewer deaths from contamination or toxic material in the inoculum. Bates and Roca have found that 7-day-old mice, on intracerebral inoculation, are just as susceptible to the local strain of virus as are Saimiri monkeys on intramuscular inoculation and that the minimum lethal dose for 7-day-old mice corresponds very closely to the minimum infectious dose for Saimiri monkeys.

When testing for the presence of virus in mosquitoes, suspensions of individual insects were inoculated into mice instead of using pooled mosquitoes because of the variation in virus content of individual mosquitoes. The rate and degree of virus multiplication in the mosquitoes after having a meal on an infected monkey were dependent upon the temperature at which the mosquitoes were kept and also upon the amount of virus in the infecting dose. When a moderately large dose is ingested, virus apparently dies out slowly in mosquitoes kept at 20°C., reaching a minimum concentration on about the fifth day. It apparently persists at this minimum level indefinitely. If the amount of virus ingested is small, the virus might drop below the threshold detectable with mice or even die out during the first five days without becoming established in the mosquito at all. When the environmental temperature was 25°C., the virus apparently reached its minimum level on the fourth day. At 30°C., the period of virus loss apparently lasts for two days. When the mosquitoes were kept for 20 hours daily at 25°C. and 4 hours at 35°C., the results were very similar to those obtained with a constant temperature of 30°C. Following these periods of virus loss, multiplication takes place slowly at 25°C. and 30°C. and combined 25°C. and 35°C., but there is great variation in time taken to reach titre necessary for transmission. At 30°C. there is sufficient virus after 10 days for transmission of infection to monkey by bite ; at 25–35°C. after 12 days ; at 25- 30°C. after 23 days ; at 25°C. after 28 days. Whether the mosquito becomes infected or not apparently depends on the events of the period of virus loss, which are presumably centred on the gut of the mosquito ; it is probably a question of whether the virus can penetrate the gut wall and get established in mosquito tissue before it dies or has been eliminated. These points are of great interest since the temperature conditions in the forest canopy, where haemagogus are found most abundantly, are subject to wide diurnal fluctuations. The marked accelerating effect of 4 hours at 35°C. is extremely important, for the results of the 25°–35° temperature alteration are certainly much more likely to approximate natural conditions than results with a constant temperature of 30°C. The 25°–35° temperature is also very favourable to the physiological processes of mosquitoes themselves, for there is greater longevity and the percentage of females laying eggs and the number of eggs laid per female are greater than at 30°C.

When mosquitoes were fed on infected Saimiri or Aotus, the percentage of mosquitoes showing virus depended directly upon the amount of virus in circulation in the host animal at the time of feeding, provided that the virus strain and environmental temperature were constant. With increasing doses the incubation gradually decreases from 18 days to a probable minimum of 10 days. It also seems probable that some individual haemagogus are more susceptible to infection than others, also that there is considerable individual variation in the time required for a mosquito to become infective. Experiments showed that it would be very difficult, if not impossible, to establish cyclic transmissions with haemagogus mosquitoes using a strain of virus that had been passaged several times through mouse brain.

F. O. MacCallum.

PELTIER, M. **Preparation of the Yellow Fever Vaccine produced by the Pasteur Institute, Dakar.** [Extract.] *Epidemiological Information Bull.* (UNRRA Health Division). Washington, D.C. 1946, Oct. 15, v. 2, No. 19, 806–8.

As a result of a recent test of the immunity produced by the injection of the yellow fever vaccine prepared by the Pasteur Institute, Dakar, this vaccine has been accepted by UNRRA as a satisfactory vaccine [see this *Bulletin*, 1946, v. 43, 1135].

The vaccine is made from the brains of mice inoculated with the French strain of virus which has been carried to the 256–258th passage in mouse brain. Mice are inoculated intracerebrally with virus, and only those mice that show definite paralysis on the fourth or fifth day after inoculation are used.

The brains are removed, pieces taken for aerobic and anaerobic culture, and the remainder stored in glass tubes at −25°C. till a number of brains have been collected. The brains are then transferred to a vacuum chamber containing calcium chloride and returned to the −25°C. refrigerator. The brains are then dehydrated under vacuum for three to four days. Perfect desiccation is said to take place. The sterile dried brains are removed and finely ground in a mortar with infusorial earth to which powdered kaolin is added. To one measured volume of brain powder two volumes of sterile inert powder are added. The mixture is again dehydrated under vacuum at −25°C. for 24 hours and a second sterility test made.

The sterile powder is then distributed into ampoules each containing 1/10 of a brain which represents 100 doses of vaccine. The vaccine titre is taken as the amount which will kill a mouse with regularity at a dilution corresponding to one part fresh virus in 1,000,000 parts. The ampoules are sealed under vacuum and stored at −4°C. The vaccine retains its potency for two months after leaving the laboratory, provided it is kept in an ice-box. The vaccine may be transported at ordinary temperatures if for not more than a few days.

For use, the powder is placed in a mortar and 2 cc. of a sterile neutral gum solution is added drop by drop and mixed with the powder. The yellow fever vaccine is frequently mixed with dried anti-smallpox vaccine virus and injected at the same time. Two drops of the suspension are deposited with a vaccine style on the skin of the deltoid region. Through each drop, two parallel scarifications of 0·5 cm. in length are made. The gum dries and provides a covering.

It is said that the method of scarification is better accepted by the African populations than is subcutaneous injection. [The respective merits of this vaccine and the 17D chick embryo vaccine have been discussed previously, see this *Bulletin*, 1947, v. 44, 73.] *F. O. MacCallum.*

PLAGUE.

MAGROU, E. Epidémie de peste bubonique à Ferryville (Tunisie). Traitement par la sulfadiazine. [**An Epidemic of Bubonic Plague at Ferryville (Tunisia). Treatment by Sulphadiazine.**] *Rev. Méd. Nav.* (*Métropole et Outre-Mer*). Paris. 1946, v. 1, No. 2, 105–21, 4 figs.

An epidemic of bubonic plague appeared in Ferryville in August 1944 and ended in March 1945. There were 37 cases, with 10 deaths. All the deaths occurred amongst men except one which was in a child. The cases comprised 24 men, 6 women and 7 children of less than 13 years old. There were 25 cases

amongst Europeans and 12 amongst the native population. Half of the persons affected were workers at the Naval Establishment of the port or members of their families.

Clinically, all cases assumed the bubonic form, except one, which was septicaemic. One patient developed a secondary pulmonary form.

Treatment with sulphadiazine reduced the mortality in 28 patients so treated to two (7·14 per cent.). The addition of therapeutic serum did not appear to offer any additional advantage. Prophylactic measures included general vaccination of the local population with Girard's live vaccine : this vaccine was given to nearly 60,000 people.

The anti-rat campaign within the naval area of the port was intensified and should not be relaxed : the hope is expressed that the civil authorities will co-operate in maintaining it. *H. J. O'D. Burke-Gaffney.*

LANDSBOROUGH, D. & TUNNELL, N. **Observations on Plague Meningitis.** *Brit. Med. J.* 1947, Jan. 4, 4–7.

Meningitis is not regarded as one of the common lesions in plague. This plague series of eight fatal meningeal cases, out of a total of 203, emphasizes the fact that unusual symptoms may lead, and have led, to incorrect diagnosis at the beginning of an epidemic. *Pasteurella pestis* was found in the cerebrospinal fluid of five of these patients and one of them, probably the most interesting, came to post-mortem examination. This eighth case had the appearance of a primary meningitis, for there was no sign of a bubo. The brain and spinal cord were covered by a thick fibrino-purulent exudate and spleen smears showed plague bacilli. Meningeal involvement in all of the cases, except the eighth, was a complication of pre-existing bubonic plague, but three of them did not show plague bacilli in the cerebrospinal fluid. There was, however, no reason to suspect that the meningeal process could be a manifestation of serum allergy. Even in the primary meningitis of the eighth case the authors admit the possibility that at some stage of the disease a bubo may have been present and that there had been transition to septicaemic plague. Another point which receives speculative comment is that " the course of the illness in all these patients was longer than usual in plague," which might have been due to energetic treatment and might have facilitated " meningeal involvement by prolonging the course of illness in those patients who would otherwise have died earlier."

W. F. Harvey.

SOKHEY, S. S. & WAGLE, P. M. **A Note on the Use of Sulphonamides in the Treatment of Plague in the Field.** *Indian Med. Gaz.* 1946, Sept., v. 81, No. 9, 343–6.

Much the most important single factor determining death or recovery in plague is the development and degree of septicaemia. In fact, if there were only bubo and no septicaemia, spontaneous recovery was the rule. It is well, therefore, in evaluating treatment to concentrate on septicaemic cases. The case mortalities in field trials, 1,604 cases, of which 1,328 related to sulphathiazole, were : with treatment antiplague serum, sulphapyridine, sulphathiazole, sulphathiazole *cum* anti-plague serum, sulphadiazine and, as controls, iodine intravenously, 50·7, 50·0, 41·6, 32·0, 20·9 and 91·0 per cent. respectively. Here sulphadiazine showed significant reduction of mortality to 20·9 per cent. as compared with the iodine control, 91·0 per cent. Suggestions are made for future field trials on a common plan to obtain statistically comparable results. Dosage of sulphonamides followed the usual lines :—sulphathiazole, an initial dose of 2 gm. followed by 2 gm. four hours later and thereafter 1·5 gm. every

four hours till the end of the first 24 hours. Continuation of therapy should not extend to more than 10 days : sulphadiazine, an initial dose of 4 gm. followed by 2 gm. every four hours, again for not more than 10 days. The temperature and pulse should have remained normal for two days. Toxic effects were few and could be reduced " if an alkaline mixture containing citrates is given every four hours after each dose of the drug and the patients encouraged to drink plenty of water so as to maintain a urinary output of 1,000 to 1,200 ccm. a day."

W. F. Harvey.

HUANG, C. H. & CHU, L. W. **Treatment of Bubonic Plague with Sulfadiazine.** *Amer. J. Trop. Med.* 1946, Nov., v. 26, No. 6, 831–9, 1 fig. [20 refs.]

Sulphathiazole is admittedly efficacious in bubonic plague. The authors, however, as a result of their experience in a small series of 25 cases are inclined to think that sulphadiazine may be even more effective. Of the 25 cases, 16 were treated with sulphadiazine alone, three with sulphadiazine and serum, four at first with sulphadiazine and serum but later with sulphadiazine, and two with sulphathiazole alone. It was apparent in this study that bacteraemia is readily controlled by the sulphonamides, but that viable bacteria remain unaffected within buboes. This, as the authors point out, leaves open the possibility of relapse and, in fact, relapse may have possibly occurred in one case. The argument for superiority of sulphadiazine over sulphathiazole is based on its use in four cases where sulphathiazole had proved unsuitable and where replacement with sulphadiazine was followed promptly by satisfactory response. Moreover, sulphadiazine has fewer toxic reactions than sulphathiazole.

W. F. Harvey.

GRASSET, E. **Control of Plague by means of Live Avirulent Plague Vaccine in Southern Africa (1941-44).** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Dec., v. 40, No. 3, 275-94. [11 refs.]

Examples of the use of live avirulent plague vaccine as a means of controlling human outbreaks are becoming numerous. In South Africa, sylvatic plague is a problem ; the enzootic area is huge, extending " from the Cape Karoo and the High Veld north-westward through the Kalahari desert to Bechuanaland, South-west Africa and Basutoland." Vigorous measures have been taken to apply vaccino-prophylaxis and to collect data during human plague outbreaks. The vaccine, of K/120 South Africa and E.V. Madagascar strains, was a live suspension in concentration of 1,000 million organisms per cc. given subcutaneously in a dose of 1 cc. by single injection. Experiments in dehydration of the vaccine at low temperatures by means of the lyophile process showed storage capabilities up to two years with " only little attenuation in the antigenic properties." As a method of mass immunization carried out to a total of 40,000 individual doses, the vaccine proved eminently satisfactory inasmuch as the reactions were mild. Fourteen outbreaks of plague have been investigated and out of one total of 24,000 persons immunized, there occurred only seven pneumonic, seven bubonic and one septicaemic case of plague. The last case recovered. Protection from the immunization is claimed to begin to be effective by the fifth day and to be maximum by the tenth day after inoculation.

W. F. Harvey.

WAYSON, N. E., MCMAHON, Margaret C. & PRINCE, F. M. **An Evaluation of Three Plague Vaccines against Infection in Guinea Pigs induced by Natural and Artificial Methods.** *Pub. Health Rep.* Wash. 1946, Oct. 18, v. 61, No. 42, 1511–18.

There is probably no better test organism for evaluation of effective prophylactic vaccine immunization than a *Pasteurella*. Plague, moreover, is a

disease communicable to animals and to man by means which are identical; and that cannot be said to be the case in very many human infective diseases. A model series of experiments is described in this article, which requires close reading. The numbers of animals used, 10 to each test, is not large but the results are clear and significant. Three plague vaccines were tested, all of them consisting of organisms killed by phenol or formalin which would seem, judging by the results, to affirm that a dead vaccine still holds the field in immunoprophylaxis. Guineapigs were the test animals, because they are extremely susceptible to plague, develop symptoms of plague in much the same way, and convalesce from plague in much the same way as man. The whole series of experiments was not only well controlled, but as nearly natural as could be, because the final test of immunity was by the bites of proved "vector" *Xenopsylla cheopis* fleas, as distinct from merely proved "infected fleas".

Cultures of plague for the preparation of vaccine were grown at 39°C. in preference to 37°C. or lower temperatures, because experience had demonstrated the greater value of these vaccines and because the plague bacillus at 39°C. developed a larger immunogenic envelope. Two sets of controls were provided, each of equal numbers of animals with the test series: these were a non-specific inoculation with anti-typhoid vaccine and no treatment at all. The evidence of successful transmission of plague on clinical grounds has been determined by several years' experience and is a very useful column of results in the tables provided and also a useful addition to the usual argument from mortality alone. This clinical evidence is given by the appearance of a red puncture point where the truly vector flea has bitten "which is surrounded promptly or within 15 to 30 minutes by a red areola of from 3 to 5 mm. in diameter . . . , the development of a red papule . . . , and the subsequent enlargement of contiguous lymph nodes with accompanying fever. . . . The evolution of the lesions produced in the immunized animals which recovered was remarkably similar to that which occurs in human cases which recover."

Details of the preparation of the vaccines are carefully given and there does not seem to be much point in adding alum precipitation to simple alcohol precipitation. Two tables and two protocols of the experiments are given and the following, Table I, gives the extremely satisfactory results obtained in "the animals which received vaccine injections and were exposed to the bites of vectors or to both vectors and infected fleas. . . ." :—

Preparation used	No. of animals tested	Clinical Plague	Death with Plague
Alcohol-precipitated vaccine	8	8	0
Alcohol-alum-precipitated vaccine	5	4	0
Commercial vaccine	8	7	3
Typhoid vaccine	8	7	6
Untreated	15	13	11

Fuller details of all the precautions taken to check the results and to ensure the validity of the experiment should be sought in the original communication.

W. F. Harvey.

KARTMAN, L. **On the DDT Control of *Synosternus pallidus* Taschenberg (Siphonaptera, Pulicidae) in Dakar, Senegal, French West Africa.** *Amer. J. Trop. Med.* 1946, Nov., v. 26, No. 6, 841–8, 2 figs.

The author has recently pointed out [this *Bulletin*, 1946, v. 43, 740] that *Synosternus pallidus* may be a plague vector in the Dakar region. The present paper describes tests of DDT treatments as a control measure, using a sticky

paper method of trapping fleas to estimate their numbers, as described in the earlier paper. Biting activity before and after treatment were also estimated by use of a human subject.

The DDT was applied as a 5 per cent. kerosene solution, either directly on the floor and lower walls or atomized in the air and allowed to settle, or else as a 10 per cent. talc dust. Controls untreated and sprayed with plain kerosene were kept under observation. The results showed a very great reduction with all DDT treatments which was sustained for at least sixty-four days. There was no great difference between the various methods of application and dosage rates above 100 mgm. per sq. ft. did not secure increased kills. The fleas were affected almost immediately and stopped biting within ten minutes. Kerosene alone gave a partial immediate kill and no evidence of persistent effect. Fleas in untreated huts remained high. *J. R. Busvine.*

CHOLERA.

STOWMAN, K. **The 1946 Cholera Epidemic in China.** *Epidemiological Information Bull.* (UNRRA Health Division). Washington, D.C. 1946, Nov. 15, v. 2, No. 21, 877–93, 1 map.

Epidemics of cholera have been an almost constant occurrence in China for the past forty years or more, but the 1946 epidemic was one of the most extensive ever recorded in the Far East. At the same time the loss of life was not so great as the early returns led the authorities to expect. Most of this Bulletin, which is to be discontinued, deals with the distribution of cholera throughout the several provinces of China. Cholera had appeared as far north as central Manchuria and inner Mongolia, as far south as Hoppo 70 miles east of the Tonking border, and westward within a hundred miles of Chungking.

Epidemiologically, it is held that two completely distinct main foci exist, and the 1946 outbreak represented two partially superimposed epidemics: the Yangtze epidemic and the Kwangtung epidemic. The former had a low, moderate case mortality rate, which leads to the conclusion that "the Yangtze type is more amenable to treatment than the Kwangtung type." The chief of the epidemiological service takes the opportunity in this report to remark on the strict compliance of China with the rules of notification. "This strict adherence to both letter and spirit of the International Sanitary Conventions entitles the National Health Administration to high esteem."

W. F. Harvey.

VAN LOGHEM, J. J. Le vibrion el Tor isolé à la Mecque. [**Vibrio El Tor isolated in Mecca.**] *Ann. Inst. Pasteur.* 1946, Nov.–Dec., v. 72, Nos. 11/12, 976–7.

GALLUT, J. Sur la détermination du vibrion cholérique: production d'acétylméthylcarbinol. [**Production of Acetylmethylcarbinol by the Cholera Vibrio.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 7/8, 239–44. [10 refs.]

Vibrios agglutinable by international standard anti-O serum are the true cholera vibrio and the El Tor vibrio. The further test of haemolytic activity and the Voges-Proskauer reaction serve to separate the two groups, true cholera being Voges-Proskauer negative. Gallut contends that true cholera is not Voges-Proskauer negative, but is capable, in a sensitive medium with suitable testing, of producing acetylmethylcarbinol. This finding, however,

does not invalidate the test, because the El Tor vibrio produces acetylmethylcarbinol in about 4 times greater quantity and its congener the Celebes vibrio in 5 times greater quantity than the cholera vibrio. In a favourable medium like Ramon bouillon containing 0·5 per cent. glucose the cholera vibrio will produce from 2 to 60 mgm. acetylmethylcarbinol per litre, and if the amount exceeds 100 mgm. this is presumptive evidence that the test vibrio is either El Tor or Celebes. *W. F. Harvey.*

BURROWS, W., MATHER, Adaline N., ELLIOTT, Marian E. & WAGNER, Sylvia M. **Studies on Immunity to Asiatic Cholera. I. Introduction.** *J. Infect. Dis.* 1946, Sept.–Oct., v. 79, No. 2, 159–67. [23 refs.]

In this Introduction to Studies on Immunity to Cholera, the authors assemble a number of data and statistical opinions on the proved, or unproved, value of cholera vaccines. They bring forward, and themselves comment on the fact, that there is little positive evidence available: a tentative conclusion may perhaps be drawn "that immunization produces an immunity of some small degree of effectiveness," but "prophylactic inoculation against cholera as practised now and in the past, leaves much to be desired." The cholera vibrio in its infection remains within the lumen of the bowel and to all intents and purposes "outside the tissues of the body throughout the disease." Even the symptoms of cholera may possibly be due as much to dehydration and demineralization as to toxaemia. [It might have been worth while advocating evaluation of the prophylactic effects of inoculation by the alternate case method, were it not probable that some form of chemotherapy may in the near future do away with the necessity of vaccinoprophylaxis.] *W. F. Harvey.*

BURROWS, W., MATHER, Adaline N., MCGANN, Virginia G. & WAGNER, Sylvia M. **Studies on Immunity to Asiatic Cholera. II. The O and H Antigenic Structure of the Cholera and related Vibrios.** *J. Infect. Dis.* 1946, Sept.–Oct., v. 79, No. 2, 168–97. [Numerous refs.]

A very important contribution to the controversy as to what is the true cholera vibrio is made in this article which should be carefully read and digested, especially as it suggests the acceptance of a new, "A", type of vibrio and the abandonment of the terms Ogawa, Inaba and Hikojima type vibrios for "AB", "AC" and "ABC" vibrios respectively. The argument is set out under the heading "Discussion"; a summary further presents its condensation and the "Conclusions" are clear and eminently acceptable. The *Vibrio cholerae* possesses H and O antigens, but "the components of the H antigen are distributed at random over cholera and non-cholera vibrios and have no differential significance." Serological analysis was largely restricted to the thermostable somatic O antigen of Inaba and Ogawa vibrios although the "intermediate" Hikojima receives due attention. The Inaba and Ogawa vibrios, as well as some of the El Tor vibrios, belong to Gardner and Venkatraman's immunological type OI. Investigation of the structure of the O antigen showed that it included only 13 components, to which were allotted the letters A to M, and of these A, B, C, D and E were associated with the Japanese type vibrios. This association was narrowed further to A, B, C, of which A was group-specific, B and C type-specific for Ogawa and Inaba vibrios. If it is accepted that these are major cholera vibrio antigens and that B and C "must occur in combination with A, it is self evident that 4 immunologic types are possible which are represented by the formulae A, AB, AC, and ABC." The A type found by the authors is a new, a fourth type, while the ABC type, obtained by inference, is the Japanese Hikojima intermediate vibrio.

Important among the conclusions reached are that :—(1) " The O group I of Gardner and Venkatraman is characterized by the presence of a group-specific antigen A." (2) " There was no immunological distinction between cholera vibrios and El Tor vibrios of O group I." Ample references to the literature are given. *W. F. Harvey.*

CHU, L. W., HUANG, C. H., CHANG, C. T. & KAO, H. C. **Sulfonamide Drugs in the Treatment of Cholera.** *Amer. J. Trop. Med.* 1946, Nov., v. 26, No. 6, 825–30. [12 refs.]

Three groups of cases came under observation in this series, all adults receiving treatment within 72 hours after onset. Intravenous infusion of physiological salt solution was used to correct dehydration and 2 per cent. sodium bicarbonate or 10–20 per cent. glucose were used whenever indicated. The sulphaguanidine group comprised 25, the sulphadiazine group 25 and the control group without sulphonamides 29 patients. One death is registered in the control group and one in the sulphaguanidine group. Claim is made that in the sulphonamide group, as compared with the controls, the " average duration of diarrhoea is shortened " and " the average amount of intravenous saline given is reduced." Little or no difference was shown in results between sulphaguanidine and sulphadiazine and neither of the sulphonamides appeared to exert any " remarkable effect on the time of disappearance of the cholera vibrios from the patients' stool." *W. F. Harvey.*

CHU, L. W. & HUANG, C. H. **Effect of Sulfadiazine on Cholera.** *Amer. J. Trop. Med.* 1946, Nov., v. 26, No. 6, 821–3.

" 1. In a cholera epidemic, 10 patients were given sulfadiazine in addition to saline infusions with 10 other patients without sulfadiazine treatment as control.

" 2. The average duration of diarrhea of the sulfadiazine-treated patients (4·6 days) is shorter than that of the controls (7·1 days).

" 3. One case of lobar pneumonia resulting in death and one case of parotitis occurred among the patients without sulfadiazine therapy.

" 4. Oral administration of fluid and alkalies in the treatment of cholera has been emphasized."

REIMANN, H. A., CHANG, G. C. T., CHU, L. W., LIU, P. Y. & OU, Y. **Asiatic Cholera. Clinical Study and Experimental Therapy with Streptomycin.** *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 631–47, 7 figs. and 4 charts. [15 refs.]

This article, which deals with experience of 2,374 cases and 392 deaths, strikes a refreshing note of scepticism in regard to some orthodox opinions. It certainly, by its questioning, invites attention and investigation. Is contamination of the public water supply the chief cause of epidemic cholera ? In the present epidemic, case-to-case transmission seemed to be a more important factor and it resembled dysentery in this respect. If there be real truth in that observation it should lead to concentration on the personal habits of the population for prevention rather than on expensive, though desirable, large scale sanitary engineering. Is the mortality of 50 to 70 per cent. among untreated patients not an exaggeration, " if all mild unrecognized cases could be included statistically " ? That issue is, perhaps, not so important as the estimates of satisfactory treatment and its results. The average duration of the disease in 56 patients treated by rehydration and remineralization alone was 4·6 days ;

of 30 patients, treated elsewhere, with sulphaguanidine, 3·8 days ; of 31 treated with sulphadiazine, 3 days ; and of 8 patients with severe attacks, treated with streptomycin, 3 days. Can the apparent shortening of the attacks with sulphonamides or streptomycin be taken as statistically significant ? An answer to this and other questions is, perhaps, contained in the statements :—(1) " Apart from the existence of endotoxin and the apparent toxemia at the onset of disease, the usual absence of fever, the clear mentality and rapid recovery suggest that dehydration, the loss of salts and the acidosis arising therefrom are far more important factors in causing the later signs, symptoms and fatalities," considering that " recovery usually comes so promptly after the restoration of salt and water while vibrios persist in large numbers in the stool." (2) " Cholera if properly treated . . . can be made much less serious than typhoid," as exemplified in the present epidemic where the duration of the attack in 140 patients was reduced to about 4 days and the mortality was only 5 per cent. (3) " If the simple administration of salty water reduces the duration of the disease to a few days and the mortality to 5 per cent., there is hardly any need for specific therapy unless it can be shown to abolish the carrier state sooner. Neither the sulfonamides nor streptomycin did." Apart from the criticism that caution is necessary before making too wide generalization from the results of treatment in one epidemic, the abstraction of this article might not be accepted as their full opinion by the authors and the argument, therefore, should be read in its entirety. More evidence of specific effect of streptomycin was given bacteriologically than clinically, for it reduced the large numbers of vibrios present in stained smears before treatment to nil after 12 or 24 hours, although cultures showed viable ones still present. The actual treatment may be described as immediate intravenous infusion of 1,000 to 2,000 cc. of warmed physiological salt solution at 60 to 100 cc. a minute, the amount being regulated by the size of the patient and the degree of dehydration as measured by the specific gravity of the blood. An addition of 300 cc. of 2 per cent. sodium bicarbonate solution was added " to combat acidosis when collapse was present or threatened." *W. F. Harvey.*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

PAGE, F. T. **Amoebiasis.** [Correspondence.] *Brit. Med. J.* 1946, Dec. 28, 1005–6.

Referring to the article by HAYWARD [this *Bulletin*, 1947, v. 44, 81] on cases of amoebiasis encountered by him in Italy, Page disagrees with that writer on certain points. Frank dysenteric manifestations were common in the Far Eastern theatres of war during active military operations, and were precipitated by the massive infection of debilitated persons suffering from concomitant bacillary infections. Sulphaguanidine stopped the diarrhoea but did not cure the amoebiasis. With unavoidably inadequate treatment the infection became chronic, the lesions became secondarily reinfected by bacteria, and successful curative treatment thus was rendered more difficult until the secondary bacillary invaders had been cleared by sulphonamide and penicillin treatment after the patients' return to the United Kingdom.

By contrast, advanced chronic cases of amoebiasis were rarely seen in India Command either during or after the war ; and since the war ended they have seldom been seen in the Far Eastern theatres of operation. Such infections

with *E. histolytica* do not differ in their course and response to treatment from those encountered elsewhere under parallel conditions ; and now, in India, the usual case is akin to that described by Hayward in Italy.

The diagnosis in a chronic case of amoebiasis with an infection localized in the caecum may not be established by examination of a dozen stools, even after purgation, and the sigmoidoscopic appearances are normal. In these cases a purely clinical diagnosis of amoebiasis followed by suitable treatment is justified by the dramatic improvement in the health which follows. *A. R. D. Adams.*

CARRUTHERS, L. B. **Pleurisy due to Amoebiasis.** *J. Trop. Med. & Hyg.* 1947, Jan., v. 50, No. 1, 12–15. [11 refs.]

" (1) The amoebic hepato-pleuritic syndrome is common at Miraj.

" (2) A series of representative cases is reported.

" (3) The presence of amoebic colitis or of amoebic hepatitis in the course of pleuritis justifies a trial of emetine in the treatment of the pleurisy."

RUSSELL, H. K., EISENHOWER, E. W. & ROOSE, D. J. **The Influence of Combat on the Incidence of Intestinal Parasites.** *U.S. Nav. Med. Bull.* 1946, Nov., v. 46, No. 11, 1716–18.

The intestinal parasites of three groups of men are compared : one group had been subjected to combat conditions on islands (Palau) which the Japanese had occupied recently ; a second group had been stationed at an advanced base for 18 months ; and the third had recently arrived from the United States as replacements. There were 100 men in each group.

A single stool was examined by " direct smears ", one in saline and one in iodine, and by a concentration floatation method. A list of the parasitic findings in the three groups is given ; this includes nine helminthic species (including *Heterodera radicicola*) and eight protozoan species. The " combat " group showed a heavier infection of all the commoner pathogenic parasites ; for example, *Entamoeba histolytica* was found in 23 of this group, compared with 6 and 3 for the " advanced base " and " replacement " groups, respectively ; and hookworm infection in 25 compared with 4 and 6. Other figures were *Giardia* 6, 1 and 3 : *Ascaris* 6, 3 and 4 : *Trichuris* 8, 3 and 2 : and *Strongyloides* 7, 0 and 1. There was a high incidence of *E. coli* and *E. nana* in all three groups, the percentages being 32, 21 and 19, and 14, 9 and 11, respectively.

Among 57 patients " admitted to the gastro-intestinal service " during the same period, the percentage infection rates of the above-mentioned parasites were *E. histolytica* 37, *E. coli* 31, *Giardia* 5, hookworm 21, *Strongyloides* 9, *Ascaris* 9, and *Trichuris* 5.

In the individuals with hookworm infections, normal haemoglobin levels were found in 34, whereas 12 were classed as suffering from hookworm disease ; these had an average of 10·4 grammes of haemoglobin per 100 ml. of blood and 3·7 millions erythrocytes per cmm. The average eosinophil counts of the two groups were 15·5 and 32·5 per cent., respectively.

These islands were very insanitary and there was a high incidence of parasitic infection amongst Japanese prisoners. Living on these islands under combat conditions naturally subjected the men to heavy infections.

[There is no suggestion in this paper that actual combat influenced the infection rate ; the title is, therefore, misleading.] *L. E. Napier.*

See also p. 470, BAROODY, **Modification of the Faust Method in the Detection of Cysts and Ova.**

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

PELTIER, M. La fièvre récurrente à poux en Afrique Occidentale Française. Epidémie ancienne.—Menaces actuelles. [**Louse-borne Relapsing Fever in French West Africa : Past and Present Significance.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1946, v. 3, No. 1, 21–7. [15 refs.]

SICAULT, G. Considérations sur l'épidémie de la fièvre récurrente mondiale au Maroc. [**Considerations on the Epidemic of Cosmopolitan Relapsing Fever in Morocco.**] *Bull. Inst. Hyg. Maroc.* 1944, v. 4, 5–25, 3 charts.

This epidemic of louse-borne relapsing fever spread from Tripolitania early in January 1945 and travelled from east to west across Morocco. The number of cases in the Protectorate gradually rose from a total of 162 in February 1945 to a maximum of 5,027 cases in January 1946. The total number of cases recorded in 1945 was 27,780, and 13,192 in the first three months of 1946. The mortality averaged 5·03 per cent. In any particular district the epidemic reached its maximum in 3 or 4 months and then rapidly diminished.

Numerous clinical varieties were observed ; about 60 per cent. of the cases relapsed, usually about a week after the initial febrile attack. Exceptionally 2, and even 3 or 4 relapses were seen. When serious complications occurred, they usually developed during the relapses. Treatment with arsenicals, especially novarsenobenzol in progressive doses—0·30, 0·45 and 0·60 gm. at intervals of 2 to 3 days—cut short the initial attack and prevented relapses in the majority of cases. The use of trivalent arsenic is not recommended, however, when hepato-renal complications are present. The distribution of food by the Government helped to check the severity of the outbreak, and the spread of the disease was stopped by the use of insecticidal powders containing DDT or Gammexane. It is hoped that by the general use of these insecticides, and their issue at a sufficiently low price to enable them to be bought by the public, this and other insect-borne diseases will disappear. *E. Hindle.*

BERGERET, C. & RAOULT, A. La fièvre récurrente à tiques à Dakar. Clinique, thérapeutique. [**Clinical and Therapeutic Aspects of Tick-borne Relapsing Fever at Dakar.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1946, v. 3, No. 1, 29–56.

YOUNG, W. A., FARR, A. G. & MCKENDRICK, A. J. **Relapsing Fever in the Lake Province of Tanganyika, with an Account of a Case in an Eight Day Old Infant.** *East African Med. J.* 1946, Nov., v. 23, No. 11, 345–7.

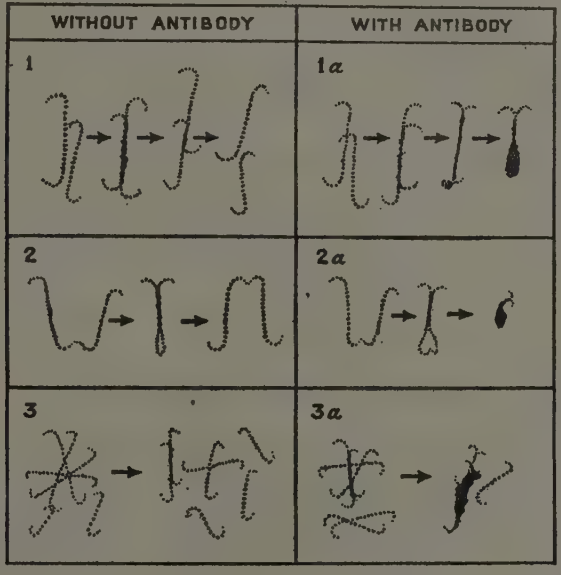
GARDNER, A. D. **Agglutination of Leptospirae.** *Lancet.* 1947, Jan. 4, 20–21, 1 fig.

The description of a simple and rapid microscopical technique for leptospiral agglutination, which has been found to give quick and reliable results in the diagnosis of Weil's disease.

Two wire loops are required, one about 3 mm. in diameter, and the other 1 mm. diameter, so as to deliver a volume about one-tenth that delivered by the larger loop. A suspension of a living culture of suitable leptospira 4 to 7 days old, in some standard medium, is used for the test. The culture should be rich enough to show at least 10 organisms in a 1/12 in. dark ground immersion field in a wet film. If it contains more than 20 per field the suspension should be diluted. The serum to be tested is used undiluted, diluted 1 in 10, and 1 in 100, respectively. With the larger loop, a loopful of the living suspension is placed on a slide and then a 1 mm. loopful of the 1 in 10 dilution of the serum, giving a

dilution of 1 in 100. A number 0 coverslip is placed over the fluid and the preparation examined under dark ground illumination. If agglutination is observed, a 1 in 1,000 dilution is tested ; if negative, undiluted serum is used. It is also desirable to test dilutions intermediate between a positive 1 in 10 and a negative 1 in 100, or positive 1 in 100 and negative 1 in 1,000, in order to obtain a sufficiently precise titration to detect a subsequent rising or falling titre.

For control purposes, it is advisable to test the culture for agglutinability



Movements of living leptospirae in fluid culture-medium : 1, two leptospirae entwining and disengaging ; 1*a*, two leptospirae entwining and becoming agglutinated ; 2, a dividing leptospira twining and untwining itself ; 2*a*, a dividing leptospira twining and tying itself into a ball ; 3, a fortuitous aggregate of leptospirae dispersing ; 3*a*, a fortuitous aggregate of leptospirae becoming agglutinated.

[Reproduced from the *Lancet*.]

with a known positive serum, if all the tests on a given day are negative. Similarly, if all the tests are positive, the culture should be tested for auto-agglutination, although this is very rare.

The author finds that this method gives results equally reliable with the usual microscopic test in which formolized suspensions of *Leptospira* are used.

E. Hindle.

Wittebolle, P. & Niemegeers, L. Photodynamie et Leptospires. [**Photodynamy and Leptospira.**] *Rev. Belge Sci. Méd.* 1942, Mar., v. 14, No. 3, 79–88. [54 refs.]

The authors studied the effect of light on the susceptibility of three strains of *Leptospira* to the action of various substances, including argoflavine, sodium salts, and compounds containing arsenic, bismuth, mercury and antimony, respectively.

The strains used included *Leptospira icterohaemorrhagiae*, *L. canicola*, and *L. biflexa*. The suspensions and mixtures were examined by dark ground illumination using an arc lamp of 4·5 amp.

In the presence of argoflavine, the *Leptospira* were immobilized approximately ten times more rapidly when exposed to the arc lamp (at 20 cms. distance) than similar suspensions kept in the dark. Thus *Leptospira* in a concentration of 1/200,000 in the dark required a period of 3 hours before being immobilized, whilst, if exposed to light, only 15 minutes. This photodynamic action was shown to depend not on any heating effect, nor on the direct effect of the visible light, or ultra-violet rays.

Leptospira were exposed to the light of the arc lamp and subsequently mixed with various dilutions of argoflavine. Even when these preparations were kept in the dark, the argoflavine immobilized the organisms as rapidly as similar dilutions exposed to light. Irradiated argoflavine was found to be no more toxic to *Leptospira* than the ordinary compound. On the other hand irradiated argoflavine, when mixed with *Leptospira* in the dark, showed the usual reduction in its germicidal properties.

The photodynamic effect is not the result of the fluorescent properties of the argoflavine, for similar results were obtained with 26 non-fluorescent substances, including compounds of sodium, arsenic, antimony, bismuth and mercury, details of which are given in tabular form.

In these experiments *Leptospira*, after becoming immobilized, were found to have lost their power of reproduction. *E. Hindle.*

ROBERTSON, K. **Weil's Disease : a Rare Condition ?** *Brit. Med. J.* 1946, Nov. 30, 810–13.

The first case of Weil's disease observed by the author occurred in July, 1936, and since then 4 or 5 cases have been seen each year, all occurring in the same area of South Hampshire. The patients included persons of all ages from 5 to 78 years, and in nearly every case the infection was the result of bathing or working in water containing the infective organism. It is assumed that the water becomes contaminated by the urine of rats infected with the disease, since in Britain about 40 per cent. of rats are carriers of *Leptospira icterohaemorrhagiae*.

The clinical symptoms are briefly described and it is emphasized that half the cases showed no jaundice at any stage, and among these the incidence of leptomeningitis was very high. Leptospirae were only once isolated—by animal inoculation of the patient's blood—but such diagnostic methods are considered unnecessary. The development of antibodies after the first 5 or 6 days, with gradual increase in titre, enables the disease to be diagnosed by serum agglutination tests. Such tests were carried out by Dr. Broom and his colleagues at the Wellcome Research Institution, and the results showed the importance of examining sera at various intervals in order to detect rising titres. At least half the cases were diagnosed within the first four days. but in the more severe cases the first positive findings were delayed for some days, up to the 8th or 9th day in fatal cases. Twelve of the patients were given anti-leptospiral serum during the first four days of illness, and one received penicillin within the first two days. All these survived, whilst out of 20 cases not treated until after the 4th day, there were six fatalities. Details are given of two other severe cases successfully treated with penicillin, supporting the view that in early stages of the disease penicillin is likely to be more useful than serum.

The author adds certain points concerning general treatment. Immediately this disease is suspected, the patient should be put on a low protein diet, fluids pressed and glucose given freely. The urine should be rendered alkaline by the

use of potassium citrate, and a careful intake and output record kept for each 12 hours. In severe cases heat and even short-wave diathermy of the renal areas is used, and sometimes hot colonic irrigation. High spinal analgesia was used in three desperate cases to re-establish renal function and succeeded in one, but not in the other two patients. Finally, the opinion is expressed that the mechanism of cortical renal ischaemia is of great importance in the aetiology of the syndrome of water and nitrogen retention seen in severe cases ; and this suggests the need for earlier use of spinal analgesia in the treatment of oliguric cases.

E. Hindle.

Boiron, H. La leptospirose existe-t-elle en A.O.F. ? [**Does Leptospirosis exist in French West Africa ?**] *Bull. Méd. de l'Afrique Occidentale Française.* 1946, v. 3, No. 1, 135–8.

The author gives a brief summary of previous work on Leptospirosis in Africa, and then describes certain cases which suggest that the disease exists in Senegal and other parts of French West Africa.

On two occasions, Llovérol at the Pasteur Institute of Kindia isolated leptospira from the blood of patients suffering from bilious complaints, but did not succeed in maintaining the organism in culture. In 1945, the author examined the blood of his laboratory animals' attendant, who had shown symptoms of jaundice associated with fever 20 days previously, and found that his serum agglutinated *L. icterohaemorrhagiae* at 1 : 100, and gave a partial reaction at 1 : 1,000. *L. canicola* was also agglutinated in similar dilutions, whilst negative results were obtained with other strains. In 1946, the blood of a dog that died with symptoms suggestive of this disease gave a partial agglutination of *L. canicola* at 1 : 100 and 1 : 1,000. The serum of a second dog dying after six days illness with symptoms of gastro-enteritis, gave complete agglutination up to dilutions of 1 : 1,000 and partial at 1 : 10,000, also complete lysis at 1 : 10 against *L. canicola*.

These dogs, and also the laboratory attendant, had never left Senegal, and the findings support the view that leptospirosis exists in this part of Africa.

E. Hindle.

Bounds, L. H. & Kingery, R. M. **Weil's Disease. Report of Eleven Cases.** *U.S. Nav. Med. Bull.* 1946, Dec., v. 46, No. 12, 1808–12.

Packchanian, A. & Price, T. G. **Coexistence of the Antibodies of Yellow Fever and Weil's Disease in Human Serum.** *Texas Reports on Biol. & Med.* 1946, v. 4, No. 3, 364–7. [11 refs.]

The authors received 94 samples of serum, from persons in Brazil, which contained antibodies as a result of attacks of jungle yellow fever ; these were examined for evidence of Weil's disease by microscopic agglutination tests against Type 1 *Leptospira icterohaemorrhagiae*. Six of these 94 sera also contained antibodies for Weil's disease, the agglutination titre ranging from 1 : 100 to 1 : 1,000 ; the reaction was prompt and complete within two hours.

E. Hindle.

LEPROSY.

Ibarra Pérez, R. & González Prendes, M. A. Incidencia de la lepra según el sexo, en Cuba. [**Sex Incidence of Leprosy in Cuba.**] Marianao, Cuba. *Rev. Sifilografía, Leprología y Dermatologia.* 1946, July, v. 3, No. 3, 117–19.

That more males suffer from leprosy than do females is a general belief and it is ascribed to the greater exposure of the former to contagion "owing to their greater social activity." Others have observed that where the occupations of men and women are the same or very similar the difference in incidence is much less marked. In such circumstances Sadi de Buen in Spain gave the ratio as 1·5 : 1 among 474 patients; in Mexico among 5,165 it was 1·3 : 1; in Cuba in 1946 it was 1·52 : 1, but the figure differed considerably in different provinces. Among ambulant cases in Pinar del Rio 1·9 : 1 (but only 67 patients were seen altogether), in Matanzas 1·7 : 1 among 134, in Oriente 1·6 : 1 among 822, in Camaguey 1·5 : 1 among 383, in Havana 1·4 : 1 among 508, and at Las Villas 1·3 : 1 among 283. But among 638 hospital patients the proportion was 2·5 male to one female.

Taking hospital and ambulatory cases together, the totals are 1,710 males to 1,125 females, or 1·52 : 1, as stated above. *H. Harold Scott.*

Dharmendra & Sen, N. R. **Leprosy Bacilli in the Nose of a Neural Case with Bacteriologically Negative Skin Lesions.** *Leprosy in India.* 1946, July, v. 18, No. 3, 88–90.

Ignacio Chala H., J. Lesiones dermatológicas y nerviosas en la lepra tipo tuberculoide. [**Cutaneous and Nervous Lesions in Tuberculoid Leprosy.**] *Rev. Facul. de Med.* Bogotá. 1946, July, v. 15, No. 1, 9–74, 18 figs. [60 refs.] English summary.

[This is a full and important paper and gives an excellent summary of the skin lesions in this type of leprosy, based on a study of over 500 cases of the disease in Colombia. No mere abstract would do it justice and those interested would do well to consult the original. The nervous lesions, though mentioned in the title, are barely considered.] The article is subdivided into six sections, exclusive of a summary and a bibliography.

Section I deals with generalities, notably the classification of types and forms of leprosy. The author is not altogether in favour of the "Cairo" classification; he prefers to divide patients into lepromatous, tuberculoid, and the non-characteristic, in which he would place the "prelepromatous" and the "pretuberculoid". Section II, which is well illustrated by 13 photographs, treats clearly and without redundancy of the dermatology of the tuberculoid lesions, in the skin and the subcutaneous cellular tissue; the infiltrated erythematous maculae, the dyschromic erythematous patches, the papular and tuberoid forms, the miliary and perifollicular lichenoid lesions and the sarcoid types and nodular elements. They differ fundamentally from the reddish pigmented maculae of the nervous form and may be classified into four main types, which may be further subdivided: i. *Macular:* infiltrated erythematous patches with well-marked border; hypochromic centres where the skin appears to be almost normal with an erythematous periphery. This is common in *formes frustes* and important for early diagnosis. ii. *Papuloid:* the papules are like those of syphilis, common in adolescents and adults, annular and they may be flat or lichenoid. iii. *Simple tuberoid:* resembling lupus vulgaris or Boeck's sarcoids. iv. *Nodular:* like the subcutaneous sarcoids of Darier-Roussy. The first three are more common than the last.

The author next treats of lesions other than those of the skin in tuberculoid leprosy, such as those of the peripheral nerves, the mucous membranes, glands and bone and the " tuberculoid leprous reaction " usually of brief duration. In Section IV the dermatological aspect of tuberculoid leprosy in infants is specially considered. In infants the nodular, papular and tuberoid forms may all be seen ; in children over two years of age the papuloid is the most common. It evolves slowly and after some months softens and lessens in size and may die away leaving only a reddish rugose macula. Later still these lose their colour, the skin becomes thin and a depressed scar-like lesion with a definite edge remains, the so-called " vermicular scar of Rabello." Other forms not infrequent in infant tuberculoid leprosy include the lichenoid with isolated or confluent follicular papules in the middle of apparently healthy skin on the arms or buttocks, associated sometimes with dyschromic patches.

Section V is devoted to the diagnosis of tuberculoid leprosy from lupus vulgaris, syphilis, erythema multiforme, seborrhoeic eczema and the tuberculides. The best aids in diagnosis are the changes in sensation, the finding of Hansen's bacillus and the lepromin test. The next Section gives brief details of 36 cases, all in adults, except one which was in a child of 8 years.

In general, this tuberculoid form of leprosy is the " clinical expression of a specific resistance to leprosy infection " and bacilli are usually few. The lepromin test is positive and diagnosis is aided by the concomitant presence of changes in peripheral sensation. The histamine test is of diagnostic value in some cases. If neuritis occurs in the tuberculoid type a neuroma, a sort of " tuberculous gumma ", will be found in the nerve involved. These tuberculoid cases are not infective and therefore constitute no menace to the public health.

H. Harold Scott.

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GARCIA MIRANDA, A. Valor de la prueba de la lepromina. [**Value of the Lepromin Test.**] *Rev. Sifilografía, Leprología y Dermatología.* Marianao, Cuba. 1946, July, v. 3, No. 3, 120–25. [14 refs.]

Several forms of antigen have been used for the intradermal test for leprosy : Mitsuda-Hayashi's lepromin prepared from lepromata and containing Hansen's bacilli and tissue débris ; bacillary lepromin, a suspension of bacilli only ; soluble purified lepromin extracted from the bacilli ; a suspension of the antigen in oil ; and 2-4-dinitro-chloro-benzene.

The results of tests by the Mitsuda and the Mantoux reactions were : In leprosy subjects, discordant. In non-leprosy subjects, the Mitsuda reaction was positive in 78 per cent., as high as that observed in countries where leprosy is endemic and the two reactions were found to coincide [see below]. In patients with cutaneous tuberculosis the Mitsuda and the Mantoux tests gave the same results. Lastly, 123 children negative to both tests were vaccinated with BCG. In a month the Mantoux reaction was positive in all but one, the Mitsuda was positive in 87 (70·7 per cent.), weakly positive in 26 (21·1), negative in 10 only (8·1 per cent.). Again, in a person believed to be free from leprosy, infection with *Myco. tuberculosis* may provoke sensitization to leprous antigen.

The author sums up his conclusions by saying that the lepromin test is of great prognostic value and is a gauge of the body's defence ; it has much value prophylactically, a negative result signifying absence of powers of resistance ; the Mitsuda reaction is an allergic one and if positive in non-lepers it is due to sensitization by *Myco. tuberculosis*. Intradermal injection with whole lepromin will bring about resistance to the leprosy bacillus, *i.e.* it is of prophylactic use ; the reaction to lepromin is of assistance in diagnosis of leprous lesions from those which may be confused with them ; dinitrochloro-benzene acts equally as well

as bacillary lepromin as an antigen; the Mantoux and Mitsuda reactions differ in a leprous patient, but in non-lepers they are coincident in 87 per cent.

H. Harold Scott.

HELMINTHIASIS.

MARCOTORCHINO, M. La bilharziose en Casamance. Réflexions d'un médecin " de brousse." [**Bilharziasis in Casamance. Some Reflections of a " Bush Doctor."**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 9/10, 361–4.

STUNKARD, H. W. **Possible Snail Hosts of Human Schistosomes in the United States.** *J. Parasitology.* 1946, Dec., v. 32, No. 6, 539–52. [16 refs.]

A review of the data concerning schistosomiasis amongst American personnel serving overseas was reported by the author in 1944. Since this report, the return of infected troops to America has focussed attention on the possibility of the disease becoming endemic in the U.S.A., and the present study, which lasted three years and which constitutes the final report to the Office of the Surgeon General of the United States Army, was undertaken to determine whether or not native North American snails can serve as intermediate hosts and transmit human schistosomes.

Laboratory bred *Australorbis glabratus* (=*Planorbis guadaloupenis*), were infected with miracidia obtained from the eggs of *S. mansoni*, and from the resultant cercariae a strain of the schistosomes was established in monkeys, Syrian hamsters, mice and rabbits. *Bulinus truncatus* was used as the molluscan host for *S. haematobium* and, rodents having proved refractory, the infection was established in baboons. For experiments with *S. japonicum*, the molluscan hosts *Schistosomophora quadrasi* and *Katayama nosophora* were bred and infected in the laboratory. Both snails proved difficult to maintain and the author describes the methods which finally proved most efficient. It is clear from the paper that laboratory animals were successfully infected with *S. japonicum*, but the species used is not stated. That the experimental infection of animals was conducted on a large scale is shown by the statement that 30 rabbits, 100 hamsters and 14,576 mice, infected with *S. mansoni*, were supplied to laboratories, which were engaged under Government contracts in testing chemical compounds against schistosomiasis. The author's techniques for infecting laboratory animals with cercariae and for exposing snails to infection with miracidia, do not appear to differ essentially from those usually employed. The following method is recommended for collecting miracidia from stools containing ova. " Eggs of *S. haematobium*, recovered from urine, began to hatch in a few minutes when placed in spring water. Eggs of *S. haematobium*, recovered from feces, did not hatch so soon and were handled by the same method as those of *S. mansoni* and *S. japonicum* which are voided only in feces. The fecal material was broken up in a beaker of water and strained through a fine-meshed wire screen. The eggs were allowed to settle and the water decanted. The washing process was repeated until the supernatant fluid remained clear. The sediment was then transferred to Erlenmeyer flasks which were filled with warm spring water, 70°–80°F. Eggs of *S. haematobium* began to hatch in 2–3 hours, whereas those of *S. mansoni* and *S. japonicum* required 12–48 hours. The liberated miracidia accumulated in the neck of the flask where they could be observed by holding the flask toward the light. This hatching technique is the surest and best method of determining the presence of viable eggs in stools." With the use of miracidia obtained from the three species of schistosomes established in the laboratory, twenty-two species of

Eastern United States snails were tested with miracidia of *S. mansoni*, twenty-five species with those of *S. haematobium* and the same number with those of *S. japonicum*. The results of these attempts at infection were consistently negative, but in the case of *Pomatiopsis lapidaria*, exposed to infection with *S. mansoni*, immature cercariae were subsequently recovered. These cercariae were not sufficiently developed to allow of their identification and, since they were recovered from snails which had not been bred in the laboratory, their presence may have been the result of a previous natural infection. The author draws attention to the fact that in the present study, only a very meagre sample of the total snail species in North America has been tested. *R. M. Gordon.*

Bedford, D. E., Aidaros, S. M. & Girgis, B. **Bilharzial Heart Disease in Egypt : Cor Pulmonale due to Bilharzial Pulmonary Endarteritis.** *Brit. Heart J.* 1946, Apr., v. 8, No. 2, 87–95, 8 figs. [12 refs.]

Report of a case.

El Ayadi, M. S. **On the Distribution of Antimony in the Body Organs during the various Phases of Intensive Treatment of Bilharzia with Repodral.** *J. Roy. Egyptian Med. Ass.* 1946, July–Aug., v. 29, Nos. 7/8, 227–37, 3 graphs.

Recent advocacy of the treatment of schistosomiasis by intensive administration of antimonials has prompted the author to investigate the distribution of antimony in the blood and internal organs after similar dosage in normal dogs and rats. Antimony estimations were carried out by the modified Gutzeit method of Boyd and Roy [see this *Bulletin*, 1930, v. 27, 570].

Dogs were treated by intensive two-day or one-day courses of " Repodral " (" Fouadin," Stibophen), and were sacrificed at intervals after the last injection. Examination of the blood and internal organs showed that antimony was concentrated in the liver ; it could no longer be detected, or was present in traces only, in the other organs 2 days after the end of treatment, and continued to be detectable in traces in the blood for a further 3 days. In the liver, however, it was still present in measurable concentration to the limit of the observation period, 7 days from the last injection.

In animals sacrificed at intervals during an intensive two-day course of treatment, a cumulative effect was clearly demonstrated (also described previously by other workers), the organs and blood showing considerably more antimony during the second than during the first day of treatment. After the last injection, the blood-concentration continued to rise, for at least 18 hours, in contrast to the concentrations in other organs, which immediately began to fall. This continuing increase in blood-concentration is ascribed by the author to the draining of antimony into the blood stream from the heavily-laden internal organs.

[For references to previous work on the distribution and excretion of antimony, after injection of various antimonials, see Goodwin and Page, this *Bulletin*, 1944, v. 41, 20.] *E. M. Lourie.*

Jaffé, R. & Ferro, R. El diagnostico de la bilharzia en el material de autopsia. [**Diagnosis of *Schistosoma mansoni* in Autopsy Material.**] *Rev. Policlinica.* Caracas. 1946, May–June, v. 15, No. 88, 189–94.

The senior author, from a study of material at his disposal, concluded that in Venezuela, in Caracas at least, the incidence of schistosomiasis was about 18, or at most 20, per cent. He was, therefore, surprised to read that at the Hospital Vargas Ottolina and Atencio had found 60 per cent. so infested [see this

Bulletin, 1944, v. 41, 945]. He and his colleague decided to study the question afresh and they examined 86 cases, one worker carrying out Fergusson's chemical method, the other histological examination of tissue from the liver and the rectum. Among the 86 there were 34 positive by the Fergusson method and 32 by the histological. They then proceeded to find out whether a positive might be given by one method and a negative by the other. In liver tissue, 11 were positive by the chemical (Fergusson) method and 29 by the histological examination ; only 4 were positive with the former but negative with the latter, whereas the opposite of this was seen in 21 cases. In the liver, therefore, the histological method is clearly the better. In rectal tissues the reverse was found ; 34 were positive by the Fergusson method and only 19 histologically ; all the histologically positive were also chemically positive, but 11 chemically positive were histologically negative.

Next, they studied which viscus was attacked with the greater frequency. Jaffé had said the liver, Ottolina and Attencio the rectum and sigmoid. Examining them by both methods, the authors found 33 in which the liver was invaded and 34 the rectum—no real difference. They maintain that the lesions of the liver (and heart) are not due to the presence of ova but to the toxins of the worms, either directly or by allergy, the latter being, in their opinion, the more likely. In the intestine the lesions are more usually diffuse, the result of the toxin of the parasite, while the ulcers are due to occlusion of the capillaries by accumulation of ova. Furthermore, the ova are mostly in nodules in the intestinal wall, or free in the tissues which show no signs of tissue reaction and, as a matter of fact, ulceration of the bowel is very rare in schistosomiasis in Venezuela. *H. Harold Scott.*

Hernández-Morales, F., Oliver-González, J. & Pratt, Caroline K. **Treatment of *Schistosomiasis mansoni* with Neostibosan.** *Proc. Soc. Exper. Biol. & Med.* 1946, Oct., v. 63, No. 1, 218–19.

There is evidence indicating that the drug has parasitotropic effects.

Kuntz, R. E. & Stirewalt, M. A. **Effects of DDT on Cercariae of *Schistosoma mansoni*.** *J. Parasitology.* 1946, Dec., v. 32, No. 6, 529–38, 1 fig.

The experiments were carried out in order to determine to what extent DDT could be relied upon for emergency schistosomiasis control, by killing cercariae and thus providing temporary protection for military personnel in endemic schistosome regions. The work was carried out with laboratory bred molluscan hosts, *Australorbis glabratus* (=*Planorbis guadaloupensis*), which were injected with miracidia of *S. mansoni*, the resultant cercariae being used to infect golden hamsters (*Cricetus auratus*).

The tests were primarily concerned with the cercaricidal properties of DDT-xylene-Triton emulsion concentrate (DDT, 20 gm. ; xylene, 60 ml. ; Triton 20 ml.). Additional tests were performed to demonstrate the toxicity of : (*a*) DDT-xylene-Triton and xylene-Triton emulsion concentrates which were diluted and aged for a period prior to use ; (*b*) crystalline or powdered DDT in water ; and (*c*) DDT applied in oil films on the surface of water. All the tests were carried out under laboratory conditions and the conclusions regarding the cercaricidal value of the various emulsions tested were based on the survival time of exposed cercariae, and on the number of worms recovered from hosts infected with treated cercariae, as compared with the number recovered from animals infected with untreated cercariae.

The authors summarize their results as follows :—

" 1. DDT (dichloro-diphenyl-trichloroethane) powder, DDT in oils and in xylene-Triton emulsions, and Triton were tested to determine their effect on

cercariae of *Schistosoma mansoni*. The results indicated that DDT alone or in any of the preparations tested was not sufficiently cercaricidal to be of practical value in the control of schistosomiasis.

"2. If DDT is to be employed (in quantities recommended for mosquito control) for the mild cercaricidal action it possesses, its action is enhanced when it is incorporated in certain emulsions. For example, the emulsifying agent, Triton, itself incapacitated or immobilized the cercariae. A mixture of Triton and xylene is more toxic than Triton alone and the mixture is made still more lethal to the cercariae upon the addition of DDT. There is a tendency toward loss of toxicity of DDT-xylene-Triton and xylene-Triton emulsions upon standing or aging in open containers.

"3. Cercariae, although severely affected and partially immobilized by DDT-xylene-Triton and xylene-Triton emulsion concentrates, are potentially infectious schistosomes until near death. A small but dangerous percentage of cercariae treated *in vitro* with the emulsions and placed in water will revive sufficiently to infect a host."

That DDT would probably prove even less efficient if tested under field conditions is emphasized by the authors who write, "In evaluating the toxicity of DDT it must be realized that tests were performed under laboratory conditions. Under such conditions the toxic agent exerts its maximum effectiveness upon the cercariae and death is further accelerated by such factors as traumatic injury by handling and alteration of temperatures (KRAKOWER, 1940, and BRADY and JONES, 1945). Obviously, in the field, dosages as tested in these experiments would be less effective because of the influencing factors common in natural waters." This is an important paper, in which the conclusions are based on a large number of carefully controlled experiments: it should be consulted in the original by all those who are interested in schistosomiasis.

R. M. Gordon.

BANG, F. B.; HAIRSTON, N. G.; GRAHAM, O. H.; FERGUSON, M. S.; SULLIVAN, R. R. **Studies on Schistosomiasis Japonica. I. Introduction** [By the authors]. *Amer. J. Hyg.* 1946, Nov., v. 44, No. 3, 313–14. **II. Methods of Surveying for Schistosomiasis Japonica** [BANG, HAIRSTON, GRAHAM & FERGUSON]. *Ibid.* 315–23, 3 figs. [12 refs.] **III. An Epidemiological Study of Schistosomiasis Japonica** [SULLIVAN & FERGUSON]. *Ibid.* 324–47, 11 figs. (1 map). **IV. Chemotherapy of Experimental Schistosomiasis Japonica** [BANG & HAIRSTON]. *Ibid.* 348–66, 4 figs. [11 refs.] **V. Protection Experiments against Schistosomiasis Japonica** [FERGUSON, GRAHAM, BANG & HAIRSTON]. *Ibid.* 367–78, 2 figs. [14 refs.]

I. The following papers are the result of studies on schistosomiasis japonica carried out from October 1944 and through 1945, in the Philippine Islands and Japan. The greater part of the work was done in Leyte, where schistosomiasis proved to be of considerable military importance.

II. Surveys for schistosomiasis may be undertaken for two purposes: to ascertain, (*a*) whether the infection is present in a community, or (*b*) if present, how much it occurs and how severe the problem is.

During this work, it has been shown that it is possible for 50 per cent. of the population to be infected and yet for the infection to be unrecognized by local physicians. The data were collected in the Visayan Group of the Philippines (Leyte and Samar) and in one well-recognized focus in Japan (Kofu, Yamanashi Province).

For the recognition of eggs in the faeces, a sedimentation method was employed by passing the emulsified stool through 3 layers of gauze in a conical urine glass. Unless this method is used a large proportion of infections will be

overlooked. An instance of this was the survey of the barrio [suburb] of Tarragona, Leyte. The first survey by direct smear showed 9 of 91 persons positive (10 per cent.) : the second, in which sedimentation was used, showed 33 of 48 (69 per cent.) positive, and there is no constant ratio between the percentage of stools found positive by direct smear and those found positive by sedimentation. In areas where the disease is not obviously present the use of a concentration method is even more important.

The average degree of liver enlargement in children of 5 to 15 years is termed the liver index. In hyperendemic areas this is high and 80 per cent. of the children have palpable livers, whilst in areas showing negative stool examinations the liver index is low ; yet correlation between palpable livers and the discovery of eggs in the faeces in one examination is not great. Studies in Japan did indicate that the liver index may form a useful guide in evaluating the significance of the disease for a community.

Existence of this disease in one particular place is proved by locating infected snails, but it was found that lack of such evidence by no means indicates that danger of contracting the disease is not present, for many soldiers were infected in a river at least a mile from any constant source of snails. Young pigs and buffalo have been found infected on Leyte. In a recent study by MAGATH and MATHIESON [this *Bulletin*, 1946, v. 43, 350] close correlation between endemicity and the percentage of infected rats was found. On Samar, in an inland valley known to be infected, all of 5 wild rats (of the *R. rattus* complex) were found to be infected, as well as a further two in an area in which the human disease did not appear to exist. This method was used in the Kofu area in Japan by SAITO [this *Bulletin*, 1935, v. 32, 627] and a marked difference found between the rate of infected rats in controlled and uncontrolled areas, whilst the rate was lower in winter than in summer.

III. The only known molluscan host of *S. japonicum* in the Philippines is *Oncomelania quadrasi*. The landing of American troops on Leyte presented a unique opportunity of studying schistosomiasis japonica and enabled a study of the epidemiology to be made in a group whose activities could be closely followed during their stay in a highly endemic area. The observations in a particular engineer battalion were particularly significant, because exposure was incurred during their normal duties. From January 1 to May 31, 1945, a total of 575 cases were recorded for Z Army units, the vast majority being diagnosed in January and February. It is believed that from the nature of exposure during engineering works, especially in bridge construction, this corps should yield a much higher incidence than in any other type of unit. Thus 35 per cent. of Z Army cases and 42 per cent. of Y Corps cases occurred in such engineer units. The relatively high proportion of the total cases in infantry could be accounted for by the great preponderance of such units.

The signal construction units were probably protected by their special clothing and boots.

In the infantry, most infections were due to swimming and washing of clothes. The overall rate in engineer troops was approximately 5 times that of the infantry.

A survey method was based on the eosinophile count and practically all men with such a count of 30 per cent., or over, were hospitalized and regarded as " schistosomiasis suspects ". It was found that such an eosinophilia was rarely due to hookworm infection.

The risk of acquiring schistosomiasis is closely related to the type of unit and specifically to the degree of exposure to fresh surface water. Although there were a number of instances in which infection was contracted from brief exposure, the great majority gave a history of prolonged exposure to stream

water, usually with few clothes. Amongst those working on bridge construction the attack rate varied from 71 to 89 per cent. in different platoons. The fact of swimming or washing of clothes in surface streams did not constitute an important factor in this particular group. Clerks and water purification workers escaped infection altogether. The evidence obtained was against ingestion of untreated water as a mode of infection.

Protection of infantry units by boots, leggings and uniform was good and accounted for the low rate of incidence of 0·5 per cent.

Failure to find *O. quadrasi* at the suspected site of exposure is no criterion of the safeness of the stream in question, and it has been shown that snails may be located considerable distances upstream from the point of human infection.

It is believed that bridge workers came into contact with cercariae whilst working in fairly deep water rather than whilst walking through swamps. The main result of this study is to emphasize the need for protective equipment in addition to rubber boots for engineer and other troops engaged in surface waters in known or suspected endemic areas.

IV. Choice of an experimental host has been one of the chief difficulties in the experimental chemotherapy of schistosomiasis and the infection of the guineapig with *Schistosoma japonicum* is the most satisfactory. The manifestations of the infection in this animal resemble those of man. The worms mature in 4 to 5 weeks so that egg-deposition in the intestinal submocosa and liver is uniformly present at 5 weeks.

The infection differs from that of human beings in that, on account of their disproportionate size, the worms cause thrombosis of the smaller mesenteric vessels. This peculiarity forms an index of the efficacy of drug treatment since thrombosis of the vessel becomes rare as the worms shrink in size during treatment.

Among the various animals treated with antimony drugs—dog, goat, rabbit, guineapig, hamster, rat and mouse—the fourth named proved most satisfactory.

Hamsters were unsuitable on account of the fat deposits along the mesenteric veins. In rats, the worms remain small and most of them stay in the capillaries which renders them difficult to detect. Infections in mice show little drug response.

Animals were infected by placing a known number of drops of a suspension of crushed infected snails (containing 100 cercariae in 6–8 drops) on the skin of the anaesthetized animal. The dosage was 3·5 mgm. of antimony per kilo. of body weight per week. The interval between treatments was a little greater where tartar emetic was used, since it had to be injected intravenously. Emetine was given intramuscularly in two 10-day courses with an 8-day rest between. The dosage was 0·02 gm. antimony per day per guineapig, corresponding to 1 gm. per day for an adult man. After ether anaesthesia the animals were exsanguinated. The liver was cut up in physiological saline and allowed to stand and the sediment examined for worms.

Findings in animals treated 4 to 6 weeks with Fouadin, tartar emetic or anthiomaline leave no doubt as to the efficacy of these drugs. Nodules in the liver are fewer, scarring is less and haematin deposits in the spleen, liver and lymph nodes less obvious.

The effects of two weeks' treatment with Fouadin showed that the whole worm was shrunken in size, and had lost most of the haematin normally present in its intestine. The ovary was reduced in size and had lost most of its cellular structure ; the vitelline gland was partly or wholly destroyed, eggs were fewer in number in the uterus, or wholly absent. Many worms had lost their hold in the smaller vessels and had migrated back towards the liver. After 4 weeks' treatment, the same changes had progressed further and degenerative changes

were present in the testes of the male. After 6 weeks' treatment, all the remaining worms were found in the liver or in branches of the portal vein.

Although the worms were rendered harmless, living specimens were capable of regenerating and of causing relapses. After 6 weeks' treatment, the number of worms recovered was 15 per cent. of the controls. Study of the eggs which have been laid in the intestine and their development gave information as to the time of drug action.

The life of the immature egg is 10 days, and if a few days more are added for the occasional survivor, the presence of such immature eggs must indicate that egg deposition has occurred within the previous 2 weeks.

After 6 weeks, the guineapigs failed to show any immature eggs, indicating that egg deposition had ceased in 4 weeks.

Among the three trivalent compounds tested, tartar emetic produced a greater decrease in the number of worms and anthiomaline and Fouadin followed in that order. Neostam given in comparable doses of weight of antimony, had little, if any, effect. Emetine, on the other hand, failed to change the average egg-count in the mucosa and in only one case were any morphological effects on the worm demonstrated. The combination of emetine and Fouadin had no special advantages. Atebrin had no effect. Antimony had no direct effect on the egg, so that the influence of these drugs on the worm and the natural life-span of the egg explain the phenomena of treatment response in human and experimental infections.

In the dog, most of the worms were located in the venules of the liver a few days after treatment started and to a lesser extent this shift also occurred in guineapig infections. Relapses in guineapigs and dogs after discontinuation of treatment, and the revivifying of the worms with gradual recovery of egg-laying capacity, explain the mechanism of relapses in human beings. Experimentally infected rats were treated with Fouadin at different periods before maturation of the worm. This was not prevented and apparently none were killed. Variation in the drug concentration in the liver was noted, but a slow response on the part of the animal was not correlated with a lower concentration of the drug.

The increased efficacy of 6 weeks' Fouadin treatment is reflected in the greater drug concentration. The higher concentration in the hamster liver is not correlated with drug effect.

V. *In vitro* and *in vivo* tests with rats suggest that troops exposed to water containing cercariae of *S. japonicum* may be afforded considerable protection. It is doubtful if any part of the body would ever be exposed to as many cercariae per unit of area as were the rats used in these experiments. Consequently in view of the 100 per cent. infection rate in all the control animals, an application which, over several hours, would prevent from 100 to 200 active cercariae from penetrating an area 2 inches in diameter might be expected to protect man for a considerable time. In the tests, in which laundry soap and dimethyl phthalate were applied after the cercariae, an exposure of 30 minutes resulted in the infection of every rat. Since these substances were shown by *in vitro* tests to be very effective cercaricides, it would appear that exposure to infested waters for only a brief period is highly dangerous. Washing exposed parts of the body with a liberal supply of soap, after even a short exposure and subsequent vigorous drying, is probably of little value in preventing infection.

Non-cercaricidal preparations such as petroleum and motor grease, offer no promise as protective agents.

Dimethyl phthalate, dibutyl phthalate, benzyl benzoate and the 45–45–10 mixture* are all effective cercaricides and will persist on the skin for a

*45 per cent. benzyl benzoate, 45 per cent. dibutyl phthalate, 10 per cent, Tween 80 emulsifier.

considerable time even after several periods of immersion. The ease with which they can be applied to the skin and the fact that they are colourless liquids without offensive odour, recommend their use.

When protection afforded by untreated clothing is considered, certain military fabrics are probably of considerable value. In all tests, olive drab woollen trouser cloth, even when old, allowed no penetration of cercariae. Even then, different samples of the same material gave different results according to the looseness or otherwise of the weave. However, during the cold season there is less chance of troops becoming infected whilst wearing woollen uniform, as the snail hosts are then hibernating.

Cotton uniforms are worn during the periods of greatest snail activity and therefore their related protective value is important. *In vitro* tests revealed that Byrd cloth is highly protective (a special cloth, first developed for cold and wind resistance and later found to be resistant to bites of mosquitoes).

Cotton khaki (8 ounces per square yard, thread count : 116 ×56 inch) and herring-bone twill (8·5 ounces per sq. yard, thread count : 72×46 per inch) allowed some penetration, even when new, but were more porous when worn.

The protection afforded by untreated cotton trouser material, that part of the uniform most likely to come into contact with cercariae, is small. The drying which takes place after exposure may diminish the risk, as cercariae are unable to live in the absence of sufficient water to cover them.

It is therefore concluded that soldiers, who enter water in uniforms impregnated with dibutyl phthalate, benzyl benzoate and 45–45–10 mixture, and who use one of these liquids or preparations containing them, for smearing exposed parts of the body, should probably be afforded a great deal of protection against schistosoma cercariae. This protection will be further enhanced, if impregnated socks are worn and the trousers kept tucked inside combat boots, thus eliminating the possibility of large volumes of water getting in directly under the bottom of the trousers to gain contact with the skin.

P. Manson-Bahr.

Hollands, R. A. & Palmer, E. D. **Observations on the Pathology of Schistosomiasis Japonica : Diagnosis by Rectal Crypt Aspiration.** *J. Parasitology.* 1946, Dec., v. 32, No. 6, 525–8. [10 refs.]

The specific diagnosis of schistosomiasis japonica is commonly made only by demonstration of eggs in the faeces. For many reasons this is often unsatisfactory and many are missed.

As in the case of *S. mansoni* the eggs are to be found in the rectal mucosa and there is much evidence that there is no definite anatomical pattern to the mesenteric distribution of the location of these two species of schistosomes.

That *S. japonicum* eggs are deposited in and emerge from as low as the rectum, even in light and early infections, has been adequately demonstrated. Soldiers who were suspected to be suffering from schistosomiasis were studied by 36 serial stool examinations and by six sigmoidoscopies with rectal crypt aspiration.

The method consists of sigmoidoscopic examination following a bowel movement, without purgative or enema. By means of a heavy-walled bent-tipped glass pipette connected with a motor-driven suction pump, developing 20 inches of mercury vacuum, any suspicious lesion was scraped and aspirated and, in the absence of lesions, this method was applied to large areas of the normal rectal mucosa. Collected material was washed back into a vial with tap water. The suspension was later spun down and sediment pipetted to a slide and examined.

Each specimen of faeces was subjected to three techniques—zinc sulphate concentration, direct smear (preferably from mucus or blood), and sedimentation by centrifugation.

Seven of 24 suspects were proved to be infected, by both diagnostic methods. Four of the seven were diagnosed by crypt aspiration alone after an average of 4·5 negative stools.

The seven proved cases were submitted to 31 sigmoidoscopies. In three, the appearances were consistently normal; the four others were marked by a variety of quickly changing superficial lesions, from the distal rectum to the limit of visualization at 25 cm. It was noted that institution of tartar emetic treatment effected no improvement until more than 0·4 gm. of antimony had been given.

The most common lesions were ephemeral clusters of dry petechiae, 1 × 1 mm., on an otherwise normal mucosa. These were located 5 to 25 cm. above the internal sphincter. This small series indicates that rectal crypt aspiration affords the most reliable and time-saving technique for diagnosing schistosomiasis japonica. *P. Manson-Bahr.*

HUNTER, G. W., INGALLS, J. W. & COHEN, Minna G. **Comparison of Methods for Recovery of Eggs of *Schistosoma japonicum* from Feces.** *Amer. J. Clin. Path.* 1946, Nov., v. 16, No. 11, 721–4.

"Our study of the comparative value of various technics in the examination of stools for ova of *Schistosoma japonicum* confirms the findings of Weller and Dammin who examined for eggs of *S. mansoni*. Their original acid-ether method was superior to previous methods and was improved on by their subsequent acid-Triton NE-ether method.

"A new sodium sulfate modification of the acid-Triton NE-ether method introduced here appears to hold promise of being the best method yet devised for the detection of eggs of *S. japonicum*. Further testing of this method should be carried out on a large scale in the field."

KATZIN, B. & MOST, H. **Cercarial Antigen (*S. mansoni*) Skin Test in Diagnosis and Management of Schistosomiasis Japonica.** *Bull. U.S. Army Med. Dept.* 1946, Nov., v. 6, No. 5, 613–16.

The authors used an antigen supplied by Oliver-González [see OLIVER-GONZÁLEZ & PRATT this *Bulletin*, 1946, v. 43, 348] and prepared from the cercariae of *Schistosoma mansoni* discharged by snails into distilled water. These were centrifuged, washed, dried, powdered and extracted in saline. The authors expected that this antigen would not be species-specific and would also give positive reactions with *S. japonicum*. This proved to be so. For the skin tests done, 0·01 to 0·02 cc. of the antigen were used at dilutions of 1 : 1,000, 1 : 5,000 and 1 : 10,000. The 1 : 5,000 dilution gave as many positive reactions as the 1 : 1,000 dilution. In a few instances the 1 : 10,000 dilution gave doubtful results when the 1 : 5,000 dilution gave positive ones. The 1 : 5,000 dilution was therefore regarded as the most suitable and it was used for the later tests. Controls were done with saline and a difference of at least 4 mm. in the diameter of the weals was considered necessary for a positive. The reactions were read 10 minutes after the injections. Erythema alone without a weal was ignored.

The results show that positive skin reactions with the 1 : 5,000 dilutions were obtained in 53 out of 54 (98 per cent.) of persons known to be suffering from schistosomiasis, 44 being infested with *S. japonicum* and 10 with *S. mansoni*. All the 39 control persons suffering from other diseases were negative.

One object of the work was to "evaluate cases" previously treated for schistosomiasis. Positive skin tests were given by 23 (40 per cent.) of 57 men

whose stools had been reported positive overseas but were negative to repeated examinations after their return to the United States. The group showing the positive reactions had had an average of 61 cc. of fouadin, while those showing negative reactions had had 48 cc., a difference without statistical significance. Nor was there any significant correlation between the results of the skin tests and the time which had elapsed since the last treatment. Culbertson [this *Bulletin*, 1942, v. 39, 355] (*Immunity against Animal Parasites*, 1941, Columbia University Press) quotes the conclusion of "Fairly and Williams" that positive skin reactions persist for years after there is no need for treatment. The skin tests done by the present authors with the 1 : 5,000 dilution of the antigen became negative in at least 60 per cent. of cases within 6 months after the end of treatment. Alves & Blair [this *Bulletin*, 1946, v. 43, 344] have reported that 85 per cent. of 53 patients treated for infestation with *S. haematobium* and *S. mansoni* developed negative skin tests to cercarial antigen 2 to 3 months after the end of treatment.

The authors did skin tests on patients suffering from schistosomiasis 30 days or more after the end of treatment, the stools and skin tests having been positive before treatment. Among these patients 49 had had 1·8 to 2·09 gm. of tartar emetic and 25 of them still had positive skin tests 30 to 90 days after the end of treatment, while 24 were negative. The stools were examined 3 times a week for 90 days or longer after treatment had ended and no positive stools were found among the 24 patients whose skin tests had become negative, while positive stools were found in 4 of the 25 whose skin tests remained positive. the treatment of these having failed. Among 31 patients treated with 100 cc. of fouadin during 14 days, 20 still had positive skin tests 30 days after the end of treatment and the treatment of 3 of these 31 had failed to produce negative stools.

The authors maintain that the skin test is easier and quicker than the examination of stools and that, although the accuracy of the skin tests is often doubted, skin tests for schistosomiasis show a high degree of specificity for trematodes. Because the skin test does become negative in many people in a relatively short time after the end of treatment with antimony, it is a valuable aid in determining whether treatment has been effective. *G. Lapage.*

Weinberg, H. B. & Tillinghast, A. J. **The Pulmonary Manifestations of Schistosomiasis caused by** *Schistosoma japonicum*. *Amer. J. Trop. Med.* 1946, Nov., v. 26, No. 6, 801–9, 3 figs.

"(1) Two cases of acute schistosomiasis caused by S. japonicum are presented. Both showed prominent pulmonary manifestations. One patient died, apparently due to tartar emetic administered intravenously in treatment, and post-mortem examination was made.

"(2) The clinical manifestations of pulmonary involvement were cough with expectoration of scant mucoid sputum, chest pain, and scattered rales of no fixed type.

"(3) The roentgenographic appearance was that of a miliary tuberculosis. In the patient who recovered there was relatively rapid and almost complete clearance during the period of observation.

"(4) Pathologically the lung examined at autopsy was studded throughout with pseudo-tubercles, each about a schistosomal ovum as a nidus. In addition a large amount of alveolar exudate, including cellular elements, was present.

"(5) It is suggested that the pulmonary manifestations seen in the first or 'incubation' stage of this disease may actually be due to the localization of ova in these tissues."

INGALLS, J. W., Jr. **The Control of Schistosomiasis Japonica. III. Studies on the Longevity of Cercariae of *Schistosoma japonicum* in Saline Solutions.** *J. Parasitology.* 1946, Dec., v. 32, No. 6, 521–4.

" Insofar as the hazard of exposure to *S. japonicum* cercariae is concerned, sea water with a 3 per cent. salinity may be considered absolutely safe for bathing, since it provides complete kill of the cercariae in less than three minutes. Areas in which sea water is diluted to less than 1·5 per cent. salinity by river waters infested with these cercariae must be considered as potentially dangerous. The exact point between sea water salinities of 1·5 per cent. and 3 per cent. where absolute safety is afforded was not determined in these tests. It will depend upon the infectivity of those cercariae able to survive for a period in such solutions."

HELWIG, E. B. & BROWN, R. G. **Clonorchiasis. Report of Two Cases.** *Amer. J. Clin. Path.* 1946, Nov., v. 16, No. 11, 714–20, 6 figs.

FRIESS. Distomatose hépatique à fasciola hépatica. Infestation familiale. [**Hepatic Distomatosis due to *Fasciola hepatica* in a Family.**] *Algérie Méd.* 1946, May–June, No. 3, 247–53.

The author describes in some detail the infestation with *Fasciola hepatica* of three members of a family resident in Algeria. The father suffered from loss of 4 kilogrammes of weight and fever varying from 37·3°C. to 39·2°C., with anorexia, an eosinophilia of 40 to 56 per cent. and 3 million red blood cells per cmm. of blood. Examination of the stools and of blood films failed to reveal parasites and a general examination failed to reveal anything likely to cause the symptoms. Eventually Hodgkin's disease was suspected; the liver and spleen were found to be enlarged. The medullogram showed 70 per cent. of eosinophiles; but no abnormal cells were found. The patient subsequently regained weight, but the liver and spleen remained enlarged. Exploratory puncture gave a fluid [presumably the cerebro-spinal fluid] containing 95 per cent. of eosinophils and some monocytes. Splenic puncture showed a great increase of eosinophils to 70 per cent., but no other abnormalities. The stools were still negative, but there was now a leucocytosis of 39,000, with 4 million erythrocytes per cmm. of blood, 70 per cent. of blood eosinophils, some anisocytes and polychromatophilia and some erythrocytes with basophilic granulations. Duodenal intubation was not possible because the patient could not swallow the sound.

Examination of the patient's daughter showed an eosinophilia of 20 per cent.; this child, who was in good health, had had taeniasis 2 years earlier. Eggs of *F. hepatica* were found in the child's stools. They were then also found in the stools of the father and the mother. The mother had 2 per cent. of eosinophils. Thus only one of these 3 persons, the father, showed symptoms, but the eosinophilia was more marked in him. He was a great lover of watercress (*cresson*) and grew it privately, hoping thus to have a hygienic supply. But his plants were derived from a natural growth of watercress and probably infected snails were transferred with them.

The differential diagnosis, prognosis and treatment are discussed. Another patient had been previously treated by the author with carbon tetrachloride. The 3 persons here discussed were treated with emetine combined with carbon tetrachloride and apparently this completely cured the father and mother but the child continued to excrete eggs until the family passed out of the author's hands. The author commends Professor Guiard's practice of giving for several

days 10 centigrammes of calomel before the stools are examined for eggs of *Fasciola* ; but he considers that duodenal intubation is the method of examination of choice. *G. Lapage.*

Addis, C. J., Jr. & Chandler, A. C. **Further Studies on the Vitamin Requirement of Tapeworms.** *J. Parasitology.* 1946, Dec., v. 32, No. 6, 581–4.

Addis, C. J., Jr. **Experiments on the relation between Sex Hormones and the Growth of Tapeworms** (*Hymenolepis diminuta*) **in Rats.** *J. Parasitology.* 1946, Dec., v. 32, No. 6, 574–80.

Godfrey, L. W. **Hepatic Hydatid Cyst causing Suprarenal Haemorrhage.** *Brit. Med. J.* 1947, Feb. 1, 181, 1 fig.

Matilla, V., Covaleda, J. & Aparicio Garrido, J. El parasitismo intestinal por vermes entre la población indigena de Fernando Poo. [**Intestinal Worm Infestation among the Natives of Fernando Po.**] *Med. Colonial.* Madrid. 1946, Dec. 1, v. 8, No. 6, 415–22, 1 fig.

Investigation of intestinal worms among the native inhabitants of Santa Isabel, Fernando Po, revealed that parasitic infection by worms was present in 93·2 per cent. of cases. *Ancylostoma duodenale* was present in 80·5 per cent. ; *Ascaris lumbricoides* in 51·4 per cent. ; *Necator americanus* in 8·7 per cent. ; *Trichuris trichiura* in 12·6 per cent. ; and *Diphyllobothrium latum* in 0·97 per cent.

Half of those affected harboured two or more worms, and, in general, although the degree of infection was high in all cases, none of them showed subjective clinical evidence of the associated disease. *H. J. O'D. Burke-Gaffney.*

Most, H., Hayman, J. M., Jr. & Wilson, T. B. **Hookworm Infections in Troops returning from the Pacific.** *Amer. J. Med. Sci.* 1946, Sept., v. 212, No. 3, 347–50. [19 refs.]

During routine stool examinations of patients admitted to a military hospital, hookworm infection was found in 6·2 per cent. of 4,300 men who had not been out of the United States and in 11·5 per cent. of 2,500 men who had served in the Pacific theatre ; the latter only are considered in this report.

In 210 of the 284 patients, the hookworm infection had been diagnosed (and usually treated) before admission : in 74 the eggs were first demonstrated in the hospital. The stools were examined by direct smear and several floatation and concentration methods, and Stoll counts were made. Treatment was by tetrachlorethylene (3 ml., occasionally 5 ml., in soft capsules) with sodium sulphate purgation the night before and two hours after the dose. Stools were collected up to 4 p.m. and the worms were separated and identified.

Among patients previously treated, the mean egg count in 17 patients with *Necator* infection was 1,900 eggs per gramme of faeces and in 28 with *Ancylostoma* infection it was 2,295 : in 15 patients who had not been treated previously, the average egg counts were respectively 2,400 and 3,600 for the two infections. The infections were thus all low ; in no case was an egg count above 9,800 eggs per gramme found.

There were no signs or symptoms that could be attributed to hookworm infection. The red cell count was below 4 million in only 10 out of 100 patients and in these the anaemia could be attributed to other causes, *e.g.* malaria. The average eosinophil count was 10·2 per cent.

Identification of adult worms showed that of 169 infections 69 were *Necator*, 87 *Ancylostoma* and 13 mixed. There is evidence that the *Ancylostoma* infections were acquired overseas.

From the notes of the previous treatments of 100 patients with unspecified hookworm infections, it was calculated that 42 per cent. were cured by one treatment, 62·2 per cent. by two, 79·1 per cent. by three, 85·7 per cent. by four, 95·0 per cent. by five and 98·7 per cent. by six treatments. Two treatments effected a 55 per cent. cure rate among 35 previously untreated patients with *Ancylostoma* infection, and an 85 per cent. cure rate among 24 with *Necator* infections. *L. E. Napier.*

Stoll, N. R., Loughlin, E. H., Harris, A. H. & Chenoweth, B. M., Jr. **A Study of Hookworm Infection in Navy and Marine Personnel on Guam.** *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 687–98.

Two groups of men were examined : Group I, composed of the Marines who formed the garrison of Guam, had arrived soon after the American re-occupation in July and August 1944 and had not been further west ; they were examined between 5 and 9 months after their arrival. Group II was composed of Marines who had been on Guam from 5 to 7 months and had previously experienced combat conditions in the Philippines (Leyte) during the rainy season.

Stool samples were obtained ; 4 ml. of faeces were added to 56 ml. of water. They were shaken with glass beads, refrigerated overnight, and mixed further the following morning. From this sample, specimens were examined for hookworm ova by Lane's DCF method and, if this were positive, egg counts were made from the same sample. In a certain number of cases worm counts were made after treatment (4 ml. of tetrachlorethylene usually).

In Group I, 1,241 men were examined ; 71 were positive by the DCF method, that is a hookworm incidence of 5·7 per cent. In Group II, 742 men were examined ; of these 253 were positive, that is a hookworm incidence of 34·1 per cent. When the data of officers were examined separately, amongst 43 of Group I no positives were found and amongst 41 of Group II the percentage incidence was 34·1, identical with that of the total group.

The data were rearranged according to period of enlistment, age, and home States of the men : tables are given. In Group I, a much higher incidence was found in men coming from the Southern States, particularly the Southern Coastal States, the incidence being 20·8 per cent. among 178 men. There was a slight trend towards lower incidence with increased age and an increased period of service. These facts, combined with the fact that the majority of worms were *Necator*, suggest that most of these infections were acquired before the individuals reached Guam, that is in the United States. There were, however, instances of *Ancylostoma* infections so that it is apparent that some new infections were acquired in Guam. In Group II, however, the majority of the infections were *Ancylostoma* (88 per cent. showed this genus), and it is apparent that most of these infections were acquired during their combat period in the Philippines.

Most of the infections were very light, although there were five times as many moderate and heavy infections in Group II as in Group I.

There was no correlation between the egg count and the haemoglobin percentage in either group. The average haemoglobin of the group in which there were no hookworm eggs found was materially the same as that of the group in which there were over 10,000 per gramme of faeces. Similarly, there was little correlation between a high eosinophilia and a high egg count. It is true that the men with the two highest egg counts showed very high eosinophil counts. On the other hand there were instances of high eosinophil counts, *e.g.* 35 per cent., with no hookworm eggs. In one such case, however, anti-helminthic treatment produced a male ancylostome ; in other cases, other helminths were the cause of high eosinophilia.

There is a high incidence of hookworm disease amongst the natives of Guam —90 per cent. ; 76 per cent. of the hookworms recovered from the natives after treatment were *Ancylostoma duodenale* and in 62 per cent. of cases this hookworm alone was recovered. But the conditions under which the Marines lived were such that infection was not common.

Leyte is known to be a very heavily infected area with a relatively high proportion of *Ancylostoma*. There, under combat conditions, there was frequent exposure to infection.

There was evidence that in certain cases infection occurred by vicarious means ; three men in Group I (predominantly *Necator* infections), who were assigned to laundry duty, showed *Ancylostoma* ova in their stools and in one particular case there was very strong evidence that he obtained his infection through his hands from soiled bed-clothing that had been allowed to stand for several days in a damp condition before being washed. This man noted itching of the skin of his hands followed by episodes of throat irritation with an unproductive cough as well as gastro-intestinal upsets.

Loughlin and Stoll (1946, in the press) have shown that it is possible to become infected from damp clothing which has been lightly smeared with infected faeces and kept for 5 days on Guam. Conditions often occurred where a man wore his own damp clothing for as long as a week, and it seems very probable that re-infection may take place in this way. There was strong evidence of this in the case of three Marines, as immature adult hookworms were recovered after treatment. These men were treated more than five months after their return to Guam following two months in the Philippines. The young hookworms were of a size that indicated that these patients had probably been infected one month previously. Both hookworm species were involved. *L. E. Napier.*

AVERY, J. L. **The Incidence of Filariasis in the Central Philippines.** *J. Parasitology.* 1946, Oct., v. 32, No. 5, 497–8.

This paper records the result of a survey of the incidence of filariasis in the native population of the San Pedro Bay (Leyte Gulf) area of the Central Philippines. The greater part of the work was done in Salcedo and Mercedes on southern Samar.

Care was taken to ensure representative sampling of both sexes of all age groups and the results are based on the examination of a single dehaemaglobinized thick blood smear. All microfilariae were identified as those of *Wuchereria bancrofti*. The incidence was as follows: —

Locality	Time of examination	Number of natives examined	Per cent. positive	Microfilariae per positive slide
Tolosa, Leyte ...	Night (9.30–11.30 p.m.)	253	2·8	8·4
Salcedo, Samar ...	Night	300	1·3	3·5
Mercedes, Samar	Night	436	9·6	27·7
„ „	Day (12 a.m.–1.30 p.m.)	353	3·4	8·6

The general low incidence is to be noted and the bloods taken at Mercedes revealed a higher incidence at night than at midday, thus indicating a nocturnal periodicity. The incidence at noon is much higher than is usually encountered in a nocturnally periodic area at midday. This then constitutes a modified periodicity as suggested by AFRICA, GARCIA and LAYCO [this *Bulletin*, 1936, v. 33, 131]. The average number of microfilariae per positive slide show that not

only was the incidence of circulating microfilariae lower during the day in the Mercedes area, but the number per volume of peripheral blood was lower.

P. Manson-Bahr.

FRANKS, M. B. **Specific Soluble Antigen in the Blood of Filarial Patients.** *J. Parasitology.* 1946, Aug., v. 32, No. 4, 400–406, 1 fig.

FRANKS, CHERNOWETH and STOLL (*Amer. J. Trop. Med.*, in the press) have tested by means of the skin test, the reactivity of antigens made from larvae as well as from adults of *Dirofilaria immitis*. These tests were done chiefly on Okinawans infected with *Wuchereria bancrofti*, but they varied so much that the author of the paper here abstracted sought an explanation of these variations. They seemed to be influenced by the clinical phase of the disease. The most striking difference observed was the fact that 90 per cent. of a group of subjects with circulating microfilariae gave positive intradermal reactions to the antigen made from the adult filariid irrespective of the degree of the microfilaraemia, while only 30 per cent. of them gave positive reactions to the microfilarial antigen. The data recorded in the paper cited above suggest one of two possible explanations: (1) The microfilariae may provide a reagent different from that provided by the adult filariid, but not a more specific one, the microfilarial antigen reacting, as did the antigen from the adult filariid, with a homologous antibody in the filarial subject; (2) the failure of the microfilarial antigen to provoke an intradermal reaction in many subjects with a microfilaraemia was probably due to the presence of circulating microfilariae which formed or absorbed the antibody produced.

The author set out to explain the variety of dermal responses noted, and carried out a number of immunological experiments which are described in detail.

The author summarizes his results as follows:—

"Two antibodies have been demonstrated; one specifically directed against the microfilariae, the other against the adult filarid. The presence of circulating soluble antigen was detected in the sera of a large number of persons who had a microfilaraemia and also in the sera of a few filarial patients who did not have circulating microfilariae. Preliminary experiments indicate that sera containing this antigen (or antigens) might be utilized for diagnostic tests in filariasis. In one experiment, the results suggest that this antigen (or antigens) appears in the blood as a tide whose ebb and flow are related inversely to the different concentrations of the microfilariae in the circulation." *G. Lapage.*

HIGHBY, P. R. **A Technique for Xenodiagnosis of Filariasis.** [Research Note.] *J. Parasitology.* 1946, Aug., v. 32, No. 4, 433–4.

The author fed *Culex fatigans* and *Aëdes aegypti* on an American marine infected with *Wuchereria bancrofti* in order to find out whether microfilariae would be more readily detected in the blood taken from the stomach of the mosquito than in blood taken from the human subject. Earlier workers have reported that the microfilariae are more numerous in the former than in the latter situation. The electrohaemometer, which measures the amount of haemoglobin per unit volume of blood, was used to compare the volume of blood in the mosquito's stomach with the volume of samples taken from the human subject. The microfilariae in the blood sample, after haemolysis in N/10 HCl were recovered by centrifuging and counted. The number of microfilariae per cc. of blood is represented by the formula $\frac{1}{V} \times \frac{R}{r} \times N$, when V is the final volume in cc. of the diluted haemolysed blood, R the number of grammes per 100 cc. of haemoglobin in the host's blood, r the number of grammes of haemoglobin per 100 cc. of diluted haemolysed blood (a sample from V) and N the

number of microfilariae recovered from V. The number of microfilariae in the blood in the mosquitoes' stomachs was counted after removal of the stomachs and haemolysis of the blood. The *Culex fatigans* and the *Aëdes aegypti* used were reared in the laboratory. The former were larger and sucked more blood ; the latter were smaller and took less blood, but had more dependable appetites. After removal of the stomach of the mosquito, the head, thorax and abdomen were examined for microfilariae which might have migrated from the stomach.

Calculations showed that the microfilariae were more numerous per unit volume of blood in the stomachs of the mosquitoes than in the blood of the human host. The ratios at each of the three feeds given to the mosquitoes were 7·4 to 1, 9 to 1 and 13·3 to 1 respectively.

The author suggests that this xenodiagnosis method may be useful for the detection of light infestations when colonies of mosquitoes are available.

A further experiment showed that several mosquitoes should be used. Ten specimens of *Aëdes aegypti* were fed on the subject and then kept in the refrigerator for 4 days. Two of these had one " worm " each in the thorax, four had one " worm " each in the stomach, one had 6 in the stomach and one in the thorax and three had none at all. *G. Lapage.*

DE SARAM, G. S. W. & PIERIS, M. V. P. **Filarial Epitrochlear Gland.** *J. Path. & Bact.* 1946, July, v. 58, No. 3, 586, 2 figs. on 1 pl.

This is an account of a Ceylonese girl of 14 who suffered from pain, numbness and loss of sensation in the right arm. Various groups of lymph glands were enlarged, particularly the right epitrochlear gland, which was moveable and tender. There was no enlargement of the liver and spleen.

At biopsy, an adult filaria could be seen in section in a dilated lymphatic channel in the gland : numerous microfilariae were lying free in the uterus of the adult. It could not be determined whether the filaria was *W. bancrofti* or *W. malayi*, both of which occur in Ceylon.

The remarkable features of the case are the absence of eosinophilia and of microfilariae in the peripheral blood ; the lack of evidence of an allergic response in the affected lymph gland ; and the absence of constitutional symptoms, despite the widespread lymphadenopathy. *H. J. O'D. Burke-Gaffney.*

SCOTT, J. A. **Observations on the Rate of Growth and Maturity of** *Litomosoides carinii*, **a Filarial Worm of the Cotton Rat.** *J. Parasitology.* 1946, Dec., v. 32, No. 6, 570–73, 1 fig. [11 refs.]

The author is interested in the development of the filarial worm (*L. carinii*) in cotton rats (*Sigmodon hispidus*). He describes methods of infecting cotton rats by the bite of the blood-sucking mite *Liponyssus bacoti*. The age of worms in the mammal is known to within ten days.

Dissecting rats at intervals and plotting the length of the largest worm in each rat, he concludes that full size (20 mm. in male worms, 80 mm. in females) is reached in some cases as early as 2½ months from infection. Worms are mature before they attain full length, for micro-filariae appear in the rodent's blood as early as the fiftieth day, when female worms have attained about half their final length. *P. A. Buxton.*

SCOTT, J. A. & CROSS, Joy B. **A Laboratory Infection of the Rat with Filarial Worms.** *Amer. J. Trop. Med.* 1946, Nov., v. 26, No. 6, 849–55.

YOUNG, W. A., FARR, A. G. & MCKENDRICK, A. J. **A Report of the Occurrence of Onchocerciasis in Manenge, Tanganyika, and in the Southern Area of Lake Victoria.** *East African Med. J.* 1946, Nov., v. 23, No. 11, 351–3.

SWELLENGREBEL, N. H. & SCHÜFFNER, W. A. P. Besmettingsproeven met oxyuriseieren uit kamerstof. [**Infection with Oxyuris Eggs from Closet Excrement.**] Reprinted from *Nederl. Tijdschr. v. Geneesk.* 1946, July 6, v. 90, No. 27, 762–4, 1 fig.

The original work of LEUCKART, proving that ingested fresh eggs of Oxyuris are capable of developing directly into mature worms in the intestine without a second host, has been frequently confirmed: his further statement that the persistence of infection due to egg laying by worms in the caecum ("enteral cycle") was an unnecessary, unproven and unlikely assumption, has not been entirely accepted. Swellengrebel and Schüffner here show that egg material, which was obtained from schoolchildren who were 100 per cent. infected, and which was already at least 3 days old gave six infections among eight volunteers. The material was washed in HCl and centrifuged; the number of eggs was counted and 40 to 80 eggs on bread were fed to the subjects of test. A preliminary daily pestle perianal test was carried out to detect freedom from spontaneous infection. The first eggs appeared in 36 to 40 days or in 50 to 53 days and excretion of worms lasted 12 to 27 days. A first conclusion from the trials is that dried egg-material, ingested or inspired, as distinct from fresh conveyance by hand from anus to mouth, can be infectious; and secondly, that oxyuriasis spontaneously disappears if finger and material infection can be prevented. The possibility of finger infection can in fact be prevented or diminished, but material infection cannot. The authors deprecate the use of laxatives and high level lavage for removal of supposititious, resident egg-laying worms; they also recommend that only persons presenting evidence of "active oxyuriasis" should be treated, as, for example, with gentian violet, butolan, lubisan etc.; and that endeavour should be made to cut down in time the usual 8-day course of treatment. Simple application of vaseline to the anal region will allay pruritus and a low-level enema will remove worms. Wearing of night pyjamas and strict cleanliness with regard to the hands should be obligatory.

W. F. Harvey.

OBER, R. E. **Trichinosis. A Review of Cases in Massachusetts from 1936 to 1945.** *New England J. of Med.* 1946, Dec. 12, v. 235, No. 24, 839–42, 1 fig. [41 refs.]

"Of 287 cases of trichinosis reported in Massachusetts from 1936 to 1945, a total of 70 are reviewed for epidemiologic, clinical and laboratory data of significance and compared with the accepted clinical picture of the disease.

"The clinical findings most frequently noted were fever, malaise, orbital edema and muscle pains. Eosinophilia was the most constant laboratory finding but must not be considered diagnostic in itself.

"The control of trichinosis, in the final analysis, can be guaranteed only by the complete cooking of all pork and pork products. New deep-freezing methods may soon be expected to aid in the lowering of infectivity of pork."

PORTWOOD, Lucile M. & SANDERS, Evelyn. **Electrophoretic and Allergenic Analyses of Fractions of Larvae of** *Trichinella spiralis*. *Proc. Soc. Exper. Biol. & Med.* 1946, June, v. 62, No. 2, 165–9, 3 figs.

The authors compare the electrophoretic and allergenic properties of acid-soluble and heat-treated fractions of *Trichinella* larvae with those of the parent

saline extracts of them. An electrophoretic analysis was made in the modified Tiselius apparatus by the moving boundary method (see LONGSWORTH and MACINNES, *Chem. Rev.*, 1939, v. 24, 271).

The allergenic properties were studied in sensitized rabbits and guineapigs. Larvae were obtained by feeding each guineapig with about 5,000 *Trichinella* larvae suspended in 20 per cent. gelatin, the larvae being recovered about 7 weeks later by artificial digestion. For further details of this technique the paper itself must be consulted.

Four to six months before the intradermal tests, rabbits were fed with 20,000 *Trichinella* larvae each. About 18 months before the tests guineapigs were fed with about 5,000 larvae each. Samples of each of the 3 fractions were filtered through fritted-glass filters and tested for sterility. Rabbits were tested with 1 : 10,000 dilutions, guineapigs with 1 : 1,000 dilutions, 0·05 ml. of the fractions being injected. The results showed that each of the 3 fractions separated into 3 electrophoretic components " in addition to an incompletely separated portion associated with component 2 and a fast-moving heterogeneous mixture. In the primary extract the heterogeneous mass represented more than 60 per cent. of the total concentration. Either acid or heat treatment removed practically all of this mixture. More material was precipitated by heating than by acidification." There was no apparent difference in the area of oedema produced by the primary extract and the acid-soluble fraction, but the heat-treated allergen produced slightly less reaction than the other two. " There is an indication that the allergen is associated with component 1 ".

For further details and for the authors' discussion of their results, the paper itself must be consulted. *G. Lapage.*

OPPENHEIM, J. M., WHIMS, C. B. & FRISCH, A. W. **Clinical and Laboratory Observations on 256 Cases of Trichinosis.** *Bull. U.S. Army Med. Dept.* 1946, Nov., v. 6, No. 5, 581–93, 1 fig. [26 refs.]

In February and March 1945, trichiniasis was acquired by 256 German prisoners of war in a camp in Michigan. Against Army regulations raw processed pork from regular sources of supply had been served in all but one of the mess halls of the camp. None of the persons eating in the single mess hall in which raw pork was not served contracted trichiniasis. It was presumed that the pork was the source of the infection. The disease was mild; probably the infestation was a light one and none of the sufferers died.

A table shows the incidence of the main symptoms. It indicates that the commonest symptoms were, in the following order, weakness in 93·7 per cent. of patients, fever in 89·8 per cent., headache in 88·3 per cent., muscle pains in 73·9 per cent., swelling of the eyelids in 70·4 per cent., sweating in 63 per cent., nuchal tenderness in 52·1 per cent. and anorexia in 41·6 per cent. Usually the periorbital oedema was the first symptom to subside; it disappeared before the eighth day of the illness. After 10 to 16 days headache and muscle pains were unusual or absent. Fever was variable, exceeding 104°F. in 8 persons, but not exceeding 99°F. in five; after the 14th day it had subsided. Weakness and malaise did not disappear until the third week. Hypertension was not observed and lymphadenopathy was too infrequent to be significant.

There was an inverse relationship of the percentage of eosinophils to the clinical severity of the disease. The authors describe three of their patients which illustrate this point. One of these was acutely ill with 8 per cent. of eosinophils on admission to hospital and 34 per cent. on the tenth day, when there had been considerable improvement. Another case was similar. The third patient had only mild symptoms, but had 67 per cent. of eosinophils on admission. A similar phenomenon has been recorded by BARTLETT (*Yale*

Med. J., 1909, v. 15, 229), by MOST and ABELES (*Arch. Neur. Psychiatr.*, 1937, v. 37, 589), by ALDRIDGE (*Amer. J. Med. Sci.*, 1931, v. 181, 312) and by DRAKE, *et al.* (*J. Amer. Med. Ass.*, 1935, v. 105, 1340).

All the authors' patients reported for duty within 6 weeks of the onset of the illness, except 33 who were retained for investigation. Treatment was symptomatic, aspirin and codeine being given for muscle pains and elixir terpin hydrate and codeine for cough. Some patients were given fluids, glucose and electrolytes parenterally. When there were no contra-indications, 1 oz. castor oil was given and the first resulting stool was examined for adult *Trichinella*, 69 patients being thus examined. The authors do not believe that any benefit results from administration of anthelmintics, sera of convalescent patients or sulphonamides, nor from parathyroid hormone, calcium compounds or irradiated ergosterol given to hasten calcification of the larval cysts. WRIGHT (*J. Lancet*, 1942, v. 62, 389) has listed 121 compounds which he tested on rats; he concluded that anthelmintics will not remove the adult *Trichinella*.

The authors, could not find *Trichinella* in the stools, gastric contents, spinal fluid or blood. The incidence of eosinophilia was high, as others have found. Only 25 of the 256 patients showed on admission less than 5 per cent. of eosinophils, but after 20 days only 3 had less than 5 per cent. A study of 33 patients during 40 days, the results of which are tabulated, showed that the eosinophilia tended to rise rapidly, varying from 11 to 40 per cent., so that, after 40 days, 76 per cent. of the 33 patients had more than 10 per cent. of eosinophils and 36 per cent. of these had more than 21 per cent.

At the time of admission the total number of white blood cells was normal, except for a small number of patients with a moderate leucocytosis or leucopenia. The Kahn test, done on all subjects, was always negative.

Periodic skin tests with various antigens were done and the results of these will be published elsewhere. A wide variation was noted in the reactions to antigens differently prepared. "The highest percentage of positive immediate reactions among the infected group of patients to skin tests was 50 per cent." The results of complement fixation tests done at intervals of 3, 6 and 12 weeks will be published elsewhere. The number of positives obtained rose until 36 per cent. of the patients tested 12 weeks after the onset of the illness were positive.

Electrocardiograms obtained from 120 patients on admission were normal. Examination of 33 patients at intervals of 10 days for 40 days showed that 5 of them developed abnormalities of the electrocardiogram, 3 of these showing transient flattening of the T waves and 2 showing moderate prolongation of A–V conduction.

Muscle biopsies were done on the deltoid and gastrocnemius muscles of 36 patients divided into 2 groups of 18 each. Group 1, examined within 45 days of the onset of the illness, were all negative, but one patient showed acute myositis. Group 2 were examined about 1 year after the onset of the illness and 12 were negative, while 5 showed muscle fibrosis and one showed encysted larvae of *Trichinella*. *G. Lapage.*

DEFICIENCY DISEASES.

DE WARDENER, H. E. & LENNOX, B. **Cerebral Beriberi (Wernicke's Encephalopathy). Review of 52 Cases in a Singapore Prisoner-of-War Hospital.** *Lancet.* 1947, Jan. 4, 11–17, 4 figs. [24 refs.]

This paper, describing 52 cases of Wernicke's Encephalopathy, the largest series yet recorded, is an important contribution to our knowledge of the aetiology of this condition.

The authors consider thiamin deficiency to be the sole cause of the syndrome and their findings provide strong evidence in favour of this and justification for the title which they have chosen.

The cases were observed in Roberts Hospital, Changi Prisoner-of-War Camp, Singapore, during 1942.

The evidence leading to the attribution of all the cases to pure vitamin B_1 deficiency was briefly :—

(1) Coincidence in time of the main wave of encephalopathy with a period when the B_1-non-fat-calorie ratio was lowest, 0·2 ; (2) Its coincidence with a high incidence of other forms of beriberi, at a time when no other deficiency diseases were prevalent ; (3) the coexistence of other manifestations of beriberi in 79 per cent. of individual cases, and (4) the rapidity and completeness of cure with parenteral injections of thiamin, even in the very small doses, up to 9 mgm., that were available. 37 patients received thiamin injections and 25 were cured ; in 9 of the 11 who died in spite of injections there was a major complicating factor. Among 15 patients who received no B_1 injections, 10 died and 5 mild cases recovered slowly on dietary measures alone.

[If, as these observations so strongly suggest, Wernicke's encephalopathy is due only to Vitamin B_1 deficiency, there remains to be explained the apparent immunity of many Asiatic peoples among whom other forms of beriberi are endemic. It may be, as de Waedener and Lennox suggest, that the cerebral syndrome is only produced by severe, *acute* deficiency, whereas the common neuritic, oedematous and cardiac manifestations arise in response to a prolonged but milder vitamin lack and that the former is relatively uncommon among eastern populations.]

There was, in almost all this series of cases, a predisposing condition interfering with vitamin intake and intestinal biosynthesis and producing a severe *acute* deficiency : a history of prolonged diarrhoea, with more than three weeks on a fluid diet, mainly water, was obtained in 45 of the 52 cases.

Clinical appearances were characteristic. Anorexia, following a period of diarrhoea, was usually the first symptom. This was followed in about a week by nausea, vomiting, disorders of visual perception and nystagmus, which was a constant finding. Mental apathy and emotional change, with insomnia, gave place, as the disease progressed, to amnesia with deepening disorientation and semi-coma. In untreated cases there was a terminal phase of coma and oculomotor palsies.

There were no facilities for histological examination of post-mortem material but typical naked-eye haemorrhages of the corpora mamillaria were seen in 8 brains examined fresh. The C.S.F. was normal in all cases examined.

Intramuscular injection of thiamin produced improvement usually within 12 hours and apparently complete physical cure in a few days ; but return of mentality to normal was slower, taking up to three months in severe cases.

Dean A. Smith.

Doucet, G. Le " Mbuaki " ou maladie de carence observée au Kwango. [**" Mbuaki ", a Deficiency Disease seen in Kwango.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1946, May, No. 5, 261–73. [25 refs.]

The disease called " Mbuaki " in the Lukala region of the Belgian Congo appears to be identical with that described by Pieraerts [this *Bulletin*, 1942, v. 39, 99 ; 1943, v. 40, 406 ; 1947, v. 44, 225] under the name of diboba, and to be similar to kwashiorkor or infantile pellagra. Mbuaki is a seasonal disease, becoming epidemic towards the end of the dry weather. The incidence is ½–1 per cent. of the population. Men are occasionally affected, but the main incidence is among infants, children, and pregnant or nursing women.

The diet of the Lukala people consists chiefly of manioc, with no beans or fish, and very little meat. It is probably grossly deficient in protein.

The earliest sign of Mbuaki is depigmentation of the hair. A little later the skin also becomes depigmented, dry, thin and scaly. Vomiting and diarrhoea are not found, but there is marked loss of appetite. Other features are oedema, tachycardia, cardiac dilatation and hypochromic anaemia. The liver is sometimes slightly enlarged, and at post mortem shows fatty degeneration.

The author rejects Pieraerts' theory of iron deficiency as the cause of the disease, and considers that protein deficiency is the most important aetiological factor. He makes the interesting suggestion that the apparent thinning and atrophy of the skin may be the result of a draining-away of skin protein to supply the needs of organs essential for life. Depigmentation is attributed to lack of substrate for the production of melanin, although sulphur deficiency may also play a part. The treatment is by a high protein diet. Intraperitoneal infusions of blood have given good results in cases that were not too far advanced.

J. C. Waterlow.

BANERJEE, S. & GHOSH, N. C. **Adrenalin in Scurvy.** *J. Biol. Chem.* 1946, Nov., v. 166, No. 1, 25–9, 2 figs.

"1. The effect of scurvy on the adrenalin content of the adrenals of guinea pigs was studied by a paired feeding technique.

"2. There was significant increase in the size and also in the adrenalin content of the adrenals of scorbutic guinea pigs.

"3. The glucose tolerance tests were performed on scorbutic guinea pigs with demedullated adrenals, on demedullated guinea pigs receiving vitamin C, and on guinea pigs with intact adrenals receiving vitamin C.

"4. The demedullated scorbutic guinea pigs gave a diabetic type of glucose tolerance curve, whereas the others showed a normal tolerance to glucose.

"5. Neither adrenalin nor inanition was responsible for the lowered glucose tolerance observed in scurvy."

SPRUE.

MILANES, F., CURBELO, A., RODRIGUEZ, A., KOURI, P. & SPIES, T. D. **A Note on Bacteriological and Parasitic Studies of the Intestinal Contents of Patients with Sprue.** *Gastroenterology.* 1946, Sept., v. 7, No. 3, 306–13, 1 fig. [10 refs.]

Whilst studying the response of persons with tropical sprue to synthetic folic acid, it was observed that, although many had intestinal parasites, they responded clinically and haematologically to folic acid, even in the absence of anti-parasitic therapy. The present paper is restricted to the bacteriological study of the stools of twenty-five patients with tropical sprue and to their intestinal parasites.

After defining the criteria in the selection of patients, who were all in an advanced stage of the disease, each patient was hospitalized and restricted to a diet containing no meat, but he was allowed milk occasionally and one egg per day. In addition to daily examinations of the faeces, the large intestine was investigated by curettage of the most altered portion of the rectal and sigmoid mucosa, the small intestine by means of the Miller-Abbott tube and by collecting samples of 3–5 cc. each from the jejunum, jejuno-ileal junction and ileum. Each specimen was examined macroscopically in the fresh state. Bacteriological

cultures were also made. Intestinal parasitic ova, cysts or adult forms were present in the faeces of 56 per cent. and in the contents of the small intestine in 12 per cent. Bacterial culture revealed a multiplicity of organisms—mostly of the normal intestinal flora. In 72 per cent. of cases, a Gram-positive non-sporulating, anaerobic bacillus—*Butyribacterium*—was observed, whilst growths of yeasts occurred in the faeces in 40 per cent.

All patients improved clinically and haematologically on 10 mgm. of folic acid in daily oral doses over a period of 45 days. Their glossitis disappeared, then appetite improved, they gained weight and experienced a feeling of well-being.

The profound change in the stools after treatment in comparison with those before treatment is remarked upon, but *pari passu* the incidence of parasites, bacteria and yeasts remained essentially unchanged in the faeces of the large and small intestines.

These parasites were Ascaris, Trichuris, Necator, the commoner non-pathogenic amoebae, Giardia and Chilomastix. *P. Manson-Bahr.*

Drew, R., Dixon, K. & Samuel, E. **Residual Defects after Sprue. A Review of 26 Cases.** *Lancet.* 1947, Jan. 25, 129–34, 10 figs. [17 refs.]

This paper has been written to discuss those cases in which the sprue process persists and a method of detecting those convalescent patients likely to relapse. An endeavour was also made to find out whether radiological and biochemical abnormalities persisted and what was their relation to the degree of clinical activity of sprue.

As previous biochemical estimation of absorptive powers of the bowel lack radiological control, they are of doubtful value, since it is uncertain whether the test meals reach the absorbing surfaces of the small intestine or are held up in the stomach, an occurrence which is a feature of sprue.

The authors have used largely radiologically-controlled intestinal intubation for giving test-meals in order to estimate the absorptive power of the bowel : a method which has proved of great value in studying its pattern and motility.

The work is therefore a combination of clinical, radiological and biochemical examination of convalescent sprue patients, and of normal healthy controls.

Among the 26 patients, 25 had returned from South East India and 1 from North Africa (an unusual sprue area). In 2 patients, symptoms developed after their return to England.

With one exception, they were treated with sprue diet and parenteral liver. At this stage all showed a high total faecal-fat content.

On clinical and haematological criteria, 12 were considered to have completely recovered, 9 showed mild, 4 moderate and 1 severe signs of sprue.

Biochemical observations.—Fluid meals containing butter-fat, glucose and barium sulphate were introduced by Miller-Abbott tube into the small intestine of the fasting subject. Thereafter the position of the meal and its progress in the bowel were checked by radiography.

The site of the tube in the bowel was determined by careful screening and by a special technique. Delivery of the meal to any required portion of the small intestine could be assured and thus ensured that lack of absorption could not be ascribed to delay in gastric motility or to inefficient pyloric relaxation.

Three types of test meals were employed :—

Meal 1 : butter 75 gm., glucose 50 gm., barium sulphate 100 gm. and water 150 ml. The ingredients were made into an emulsion, warmed to body temperature.

Meal 2 : butter 31 gm., toast 2 oz., milk 2 oz., and a cup of tea were given by the mouth and followed in four hours by meal 3.

Meal 3 : glucose 50 gm., glycine 25 gm., barium sulphate 50 gm. and water 100 ml. given by mouth four hours after meal 2.

The first was given to most of the patients and allowed the rate of absorption of fat and carbohydrate to be studied. The high content and unpalatability would cause gastric delay, if given by the mouth, so meal 2 was used in such cases. Meal 3 allowed the rate of absorption of glucose and amino-acid to be studied in patients already subjected to meal 2.

Test meals were given after an overnight fast. On the meal morning, venous and capillary blood samples were taken, the latter at half-hour intervals up to four hours after the meal. Special attention was paid to correlation between the serum-lipid fractions and the number of particles (chylomicra) seen with dark-ground illumination. Increase in serum opalescence was of equal value to the chylomicron count as a criterion of lipid absorption.

Total fatty acid was determined after saponification of an alcohol-ether extract of serum by a titrimetric method developed in the laboratory. By this method (for the details of which the paper must be consulted in original) serum, 2 ml., sufficed for estimation of all the lipid fractions.

Lipoid phosphorus was estimated after incineration of a 10 ml. sample of the original alcohol-ether extract.

Non-phospholipoid fatty acid was obtained by subtracting the phospholipoid fatty acid in milli-equivalents from the sum of the total fatty acid added to 18 per cent. of the phospholipoid in milli-equivalents.

Neutral fat was evaluated as glyceryl trioleate corresponding to non-phospholipoid fatty acid.

Total cholesterol was determined colorimetrically on an aliquot of the original alcohol-ether extract after evaporation to dryness.

Particle counts were made with dark-ground examination of both venous and capillary specimens of serum according to the method of FRAZER and STEWART (*J. Physiol.*, 1939, v. 95, 21 pp.)

Opalescence of serum was recorded on a qualitative basis. In general the fasting serum was crystal clear, but was highly opalescent after fatty meals. These observations agreed with the chylomicron counts.

Blood sugar was estimated every half-hour in capillary specimens.

Amino-acid nitrogen was estimated only after meals containing glycine.

Absorption of meals.—Those introduced into the jejunum were followed by variable and inconstant absorption of fat. Glucose was satisfactorily absorbed from all parts of the small intestine.

Meals placed in the first and second parts of the duodenum gave satisfactory fat-absorption. When meals were introduced by tube at lower levels, fat-absorption appeared to depend on the extent of regurgitation into the second part of the duodenum.

Meals taken by mouth were followed by fat-absorption, but this was delayed if large amounts of fat were included, and even when a light fatty meal was given fat absorption was sometimes delayed. Meals by mouth were used chiefly for studying amino-acid absorption.

Absorption of fat.—Results with meals introduced into the first and second parts of the duodenum are considered in this respect.

They were followed by increase in neutral fat, particle counts and opalescence of the serum.

The figures for neutral fat, calculated from the values for non-phospholipoid fatty acid, show that this is the only serum-lipid which shows constant increase accompanying fat-absorption.

No significant alterations in lipoid phosphorus and cholesterol were observed ; and the increases in particle counts and serum opalescence thus accompany increase in neutral fat and afford convenient indications of fat-absorption.

Ten (of the 14 investigated) showed significant increases in blood fat content after fatty test-meals. In seven of these significant increases in chylomicron counts were observed. In the remaining 4 patients no significant rise in blood-fat was observed and in two neither visible lipaemia nor increase in chylomicron counts were observed, although fat-absorption was deranged. Thus deficiency of fat-absorption was not detected in most patients.

Absorption of glucose.—In general, the blood-sugar level rose abruptly and was followed by a sharp fall. Absorption was rapid and seen to follow equally meals introduced into the duodenum and into the jejunum. Occasionally a flattened type of blood-sugar curve was obtained, even in normal subjects.

Absorption of amino-acids.—The glycine was generally given as a separate test-meal by mouth (meal 3) four hours after the small fatty-meal (meal 2), also given by the mouth. In all 4 patients investigated satisfactory absorption of amino-acids was observed, as in normal controls.

Radiological appearances.—The technical difficulties of passing a Miller-Abbot tube were overcome by introducing 1–2 cc. of metallic mercury into the balloon of the tube, with the subject lying on his right side ; negotiation of the tube through the pylorus was thus assisted.

A large fatty meal introduced into the normal small bowel did not produce radiological appearances similar to those seen in sprue. This appears to invalidate the hypothesis of KANTOR (*American J. Roentgenol*, 1939, v. 41, 758) and STANNUS [this *Bulletin*, 1943, v. 40, 259] that the radiological changes in sprue are secondary to the abnormal fatty contents in the small intestine.

A large fatty meal introduced directly into the small bowel did not lead to slow sluggish passage as in established sprue, but the rate of transit appeared to be increased. The mucosal pattern in the jejunum was coarser than normal, suggesting that these changes are secondary to reflex stimulation.

The radiological appearances of the small bowel have been the subject of considerable attention in recent years and it has been proved by GOLDEN (*Radiology*, 1941, v. 36, 262) that the appearances, though characteristic, are *not* specific for sprue.

By their special method the authors record four types of changes in sprue :—

Changes in Motility.—In the early stages the meal passes through the small bowel more quickly, but in a well-developed case delay is the outstanding feature. When given by the mouth there is gastric retention of the meal. The unchanging appearance in the small bowel wall merits the term "moulage pattern" bestowed upon it.

Changes in Tonicity.—Areas of hypertonicity (segmentation) alternate with areas of hypotonicity (dilatation). These changes are most obvious in the middle third of the ileum. The terminal ileum is not involved to the same degree.

The tonicity of the muscularis mucosae is greater in the early stages of sprue and may be responsible for exaggeration of the jejunal pattern. Later, hypotonicity is partly responsible for the flattening, thinning, and loss of haustral markings.

Pattern changes in the mucosa are most clearly seen in the mid-third of the small bowel and are best demonstrated by spot-mucosal relief pictures after barium-sulphate solution has been delivered through a Miller-Abbott tube.

The normal feathery mucosal pattern is replaced by a coarse irregular pattern. The valvulae conniventes are widened, coarser and further apart.

They also cease to have the fine delicate appearance and are very irregular in outline.

The barium meal loses its smooth uniform consistence and is aggregated into floccules. The mucosal folds become obliterated in the terminal phases.

A moderate degree of dilatation of the colon is often present in sprue. This feature cannot be used in the differentiation of sprue from coeliac disease.

P. Manson-Bahr.

DARBY, W. J., CHERRINGTON, Mary E. & RUFFIN, J. M. **Plasma Tocopherol Levels in Sprue.** *Proc. Soc. Exper. Biol. & Med.* 1946, Nov., v. 63, No. 2, 310–12, 1 fig. [12 refs.]

"Three patients with sprue in relapse or early remission were found to exhibit very low plasma tocopherol levels. The rise in plasma concentration of tocopherols following an oral dose of 600 mg. was less in a patient with sprue in relapse than in 7 healthy subjects. The average concentration of plasma tocopherols was essentially normal in 17 sprue patients treated with liver extract for long periods. These findings are of interest in view of the recognized occurrence of deficiencies of other fat-soluble vitamins in sprue."

MANSON-BAHR, P. & CLARKE, O. **Folic Acid in Tropical Sprue. Report of a Case.** *Lancet.* 1946, Dec. 21, 903–4, 3 figs.

A man, aged 27, left England for India in March 1943. Eleven months later he developed steatorrhoea, but he went into Burma with the Chindits for three months, where he was treated for his diarrhoea with three courses of sulphaguanidine. By August 1944, he had lost over 4 stones in weight; he was then put on a milk and fruit diet, liver extract orally and by injection, and nicotinic acid. His condition improved, but steatorrhoea persisted until after his return to this country and his discharge from the Army twelve months later. At this time his weight was 2½ stone below normal. During the next year, in civil life, in spite of dietary adjustment and liver injections, his condition declined. In September 1946 he entered the Albert Dock hospital weighing 7 st. 1 lb., 3½ stone below his normal, with gross manifestations of classical sprue, marked steatorrhoea, achlorhydria and a megalocytic anaemia (red cells 2½ million per cmm., haemoglobin 50 per cent.). Dietary treatment, with injections of Plexan 4 cc. daily, and nicotinic acid 100 mgm. and riboflavine 3 mgm. daily, did not effect material improvement during his first week in hospital.

Folic acid, 10 mgm. daily, was then given by mouth for 5 days and the other drugs were stopped. The action of the folic acid was dramatic. By the fourth day the patient felt better than he had done for months, and he was soon allowed ordinary hospital diet. By the seventh day the steatorrhoea and looseness, the sore tongue, and other symptoms and signs of active sprue had disappeared; by the tenth day the patient was convalescent; and a fractional test meal a couple of weeks after beginning folic acid treatment showed a normal acid gastric juice. At the end of a month he had put on 30 lb. in weight, his stools were normal in bulk and in fat content, and his haemoglobin had risen by 30 per cent. This rapid and satisfactory response to treatment is ascribed to the folic acid, and the improvement has since been maintained. Folic acid appears to have arrested the vicious circle, after which further recovery continued without its aid.

A. R. D. Adams.

LOPEZ, G. G., SPIES, T. D., MENENDEZ, J. A. & TOCA, R. L. **Folic Acid in the Rehabilitation of Persons with Sprue.** *J. Amer. Med. Ass.* 1946, Dec. 14, v. 132, No. 15, 906–11, 6 figs.

Macrocytic anaemias are worldwide. In the past it has been considered necessary to distinguish between those cases due to dietetic failure (nutritional

macrocytic anaemia) and those due to a primary disturbance of the alimentary tract (Addisonian pernicious anaemia and sprue).

In an extremely large series it is possible to find persons whose symptoms are difficult to classify in any clear syndrome. Sometimes the same patient may suggest different syndromes when seen on different occasions. Folic acid may be expected to exert an effect on macrocytic anaemia when in relapse, irrespective of the presence or absence of steatorrhea, achylia, pellagra, etc. It also appears that thiamin, nicotinic acid and riboflavin are not capable of initiating blood regeneration and do not supplement folic acid therapy from this standpoint. In patients with any kind of macrocytic anaemia, deficiencies of these vitamins and iron not infrequently coincide and sometimes there is also a superadded factor in parasitic infections—all these complications render this research tedious and difficult. Since the introduction of folic acid the prospect is entirely different.

In the present report it has been shown that persons with sprue can be rehabilitated by the use of folic acid. After its administration there was prompt regeneration of the blood and a tendency of the alimentary tract to return to its normal functions, despite the fact that in some no antiparasitic treatment was administered, even when it appeared necessary. The desirability of prescribing a diet adequate in protein, vitamins and minerals is stressed. Among 18 patients thus rehabilitated, five were women who have resumed their household duties. Nine out of 13 men have returned to work. One of these four is a cripple, the other three, who are 75 years of age, have retired.

After the various base line determinations which were considered necessary, folic acid was administered orally in water suspension between meals. It was prepared by mixing it to a smooth paste with 4 to 5 drops of cold water and then adding 20 cc. of cold water whilst the mixture was being constantly stirred. After this material had been drunk, a small amount of water was used to rinse the glass and this was again imbibed to ensure the maximum intake of folic acid.

During the latter part of the study, the drug became available in tablet form, then 100 mgm. were administered *twice* daily. Subsequently the dosage was reduced to 100 mgm. daily and then to 25 mgm. daily but from cases studied later it was found that 5 to 10 mgm. daily is just as effective as the larger doses. *P. Manson-Bahr.*

HAEMATOLOGY.

Jersild, M. & Meulengracht, E. Bemaerkninger om "folic acid" og dets virkning ved perniciøs anaemi. [**Effect of Folic Acid in Pernicious Anaemia.**] *Nordisk Med.* 1946, Dec. 20, v. 32, No. 51, 2935–8, 3 figs. [36 refs.] [Summary in English by the author.]

"A short account is given of the experiments which led to the discovery of folic acid and the clinical use of the drug.

"Three cases of pernicious anaemia were treated with folic acid either with intramuscular injections or by mouth (15–30 mgs. daily). All cases gave a reticulocyte-response and an adequate increase in erythrocytes and hemoglobin. Also the general clinical condition improved."

Merchant, S. M. **Erythroblastic Anaemia of Cooley with a Case Report.** *Med. Bull.* Bombay. 1946, Nov. 23, v. 14, No. 22, 261–4.

VENOMS AND ANTIVENENES.

LEESON, F. **Snake Species recorded in the Gold Coast.** *Ann. Trop. Med. & Parasit.* 1946, Dec., v. 40, Nos. 3/4, 325–9.

BONSMANN, M. R. Zur Frage der Wirksamkeit von Schlangengiften bei innerlicher Darreichung. [**The Action of Snake Venoms administered Internally.**] *Arch. f. Exper. Path. u. Pharm.* 1942/43, v. 200, 167–75. [Refs. in footnotes.]

BONSMANN, M. R. Ueber die Verwendbarkeit von tropischen Pflanzenauszügen gegen Schlangenbisse. [**The Effect of Tropical Plant Extracts against Snake Bite.**] *Arch. f. Exper. Path. u. Pharm.* 1942/43, v. 200, 414–18. [27 refs.]

SOLIMAN, H. S. & MOHAMED, A. H. **Effective Agent against Scorpions.** [Correspondence.] *Lancet.* 1947, Jan. 11, 83.

Scorpions exposed to 1–4 gm. of powder containing only 1 per cent. Gammexane in talc are paralysed within 30 to 60 minutes.

DE OREO, G. A. **Dermatitis Venenata resulting from Contact with Marine Animals (Hydroids). Report of Cases.** *Arch. Dermat. & Syph.* 1946, Dec., v. 54, No. 6, 637–49, 9 figs.

DERMATOLOGY AND FUNGUS DISEASES.

BENEDEK, T., with the collaboration of I. LEWE, H. PRICE & A. KORANSKY, and with the technical assistance of Flora VAN HORN. **Pompholyx (Epidermophytosis, Dermatopyhytosis, Ringworm of the Feet, Infectious Eczematoid Dermatitis or Ringworm, Dyshidrosis). A Statistical Contribution to the Solution of the Pending Problems.** *Mycopathologia.* The Hague. 1943, Aug. 30, v. 3, Nos. 3/4, 240–54. [Numerous refs.]

This paper commences with an interesting, though dogmatic, discussion on points of historical interest. The authors castigate Tilbury FOX (*Amer. J. Dermat.* 1873, v. 4, 1) for his error in connecting this vesicular eruption with the sweat glands and naming the disease " dysidrosis " and several modern authors for their retention of the more correct name " dyshidrosis " ; they prefer the name " pompholyx " as suggested by Jonathan HUTCHINSON in 1864 (*Lancet*, 1876, v. 1, 618 : 630) although they consider that the word is as meaningless as " syphilis ". It is unfortunate that on every alternate page of their article " pompholyx " is misspelt " pompholix."

Their main thesis is that Marie KAUFMANN-WOLFF (*Dermat. Ztschr.*, 1914, v. 21) and many subsequent authorities were heretical (in the medical sense) in attributing the eruption to fungous infection of the skin ; further, the " theory of the etiology and pathogenesis of pompholyx as an exogenous bacterial, yeast or fungous infection is a complete error built up on a long series of fallacies."

The authors survey the literature of the subject ; and turning from pompholyx they suggest " that hyphomycetes do not play any causative rôle in the group of ' epidermophytosis '." They then describe an investigation of 983 persons, 4·1 per cent. of whom were negroes. Pompholyx, of the feet only, was found in 18 instances and only in white persons. Somewhat surprisingly, in making a clinical diagnosis, they considered the slightest scaling

between the toes as evidence of the malady—a criterion with which few authorities would agree. On microscopic examination, fungi were not found in the lesions, but on cultures certain moulds, yeasts and bacteria were grown but these were not classified as " pathogens ".

Having satisfied themselves that pompholyx was not due to fungous infections they admitted all the persons with clinically positive signs of pompholyx (" epidermophytosis ") without any restriction to the camping season. " We discarded all the usual proscriptions in the camp. Children and grownups ran barefooted on the fat grass of the camping ground as much as they liked. They used the same locker rooms, the same runways, shower rooms, etc., altogether.

" We discouraged ' prophylaxis ' directed toward attempts to kill the ' fungi ' or to prevent their ' dissemination '. We discarded the farcial (*sic*) ritual of ' foot-bath ' containing 1 per cent. sodium hypochlorite recommended from different quarters for use in locker rooms or before leaving the swimming pool runway in order to prevent dissemination.

" And the result ? There was no increase of incidence in ' epidermophytosis ', no spread, no dissemination and no outburst of an epidemic. And all that in a camp where nearly a thousand children and grown-ups took turns in groups every ten days in mid-summer from early June to late August."

[This paper is scarcely one to recommend to students, for there seems to be considerable difference of opinion between the authors and most dermatologists as to the signs of fungous infection and the signs of pompholyx. Nevertheless, most of us will agree with the main contention, that in the majority of cases pompholyx is not due to fungous infections of the skin.

This paper comes, in part, from the Salvation Army Free Dispensary, and it is interesting, therefore, to find that the authors have revived the art of polemics in medical literature.] *R. M. B. MacKenna.*

Alfonso Armenteros, J. Tratamiento local de las tiñas del cuero cabelludo. (Segunda nota.) [**Local Treatment of** *Tinea capitis.*] *Rev. Sifilografía, Leprología y Dermatología.* Marianao, Cuba. 1946, July, v. 3, No. 3, 133–6.

Local applications, it is claimed, have the advantage over such methods as depilation, by X-rays or the use of thallium salts. For comparison the author has divided his ten cases into two groups : one he treated by painting with a preparation containing salicylic acid 10 gm., gentian violet 2 gm., alcohol 100 cc. ; the other by an ointment containing salicylic and benzoic acids each 5 gm. in 25 gm. each of codliver oil and lanoline. Whichever was used, application was made twice daily after soaping applied with a tooth-brush, rinsing in running water and vigorous rubbing with cotton-wool soaked in alcohol. Four of the five patients treated with the paint were cured in 2–3 months (this includes the time for growth of hair over the area treated ; the lesions were free of scales and diseased hairs in 15–20 days). In the fifth case the diseased hairs were still visible after 30 days' treatment ; this patient was cured by subsequent application of the ointment. All those treated from the first with the ointment made a good recovery, the scales, crusts and diseased hairs disappeared in 15–27 days. In some who used the paint there was abundant scale and crust formation, which impeded the action of the medicament. For such patients both preparations were used, one in the morning, the other in the evening. Diseased hairs were not plucked out in the usual way with forceps because the soaping and subsequent friction effectually got rid of them.

H. Harold Scott.

PLUMMER, P. J. G. **Actinomycosis. Histological Differentiation of Actinomycosis and Actinobacilliosis.** *Canadian J. Comp. Med.* Gardenvale, Quebec. 1946, Dec., v. 10, No. 12, 331–7, 4 figs. [10 refs.]

HICKS, J. D. **Chromoblastomycosis : Report of a Case.** *Med. J. Australia.* 1946, Nov. 16, v. 2, No. 20, 705–6.

"A third case of chromoblastomycosis occurring in Australia is reported. A brief outline of the condition is given, and attention is drawn to the relevant literature."

ROSENTHAL, S. R. & ROUTIEN, J. B. **The Infectiousness of Coccidioidomycosis.** *Science.* 1946, Nov. 22, 479.

In coccidioidomycosis, infection is caused by inhalation of the spores of the *saprophytic* growth of *Coccidioides immitis* carried with the wind-borne dust of the desert. Transmission of the disease directly from man to man is almost unknown. However, to test the possibility of transmission of the parasitic form of the fungus from man to man, the authors conducted experiments in which morbid material containing the parasitic "spherules" of the fungus was instilled into the bronchi of guineapigs, and, "by applying a minimal amount of air pressure" the infective material was carried into the bronchioles and alveoli. In all the animals inoculated, a pneumonic coccidioidomycosis developed, with involvement of the hilar lymph nodes, but no extension to other organs.

From these observations the authors conclude that the parasitic form of the fungus is infectious through the respiratory tract and "all active human cases of primary or secondary coccidioidomycosis should be considered contagious until proven otherwise." *J. T. Duncan.*

HAYNES, D. M. & HESS, W. I. **Cutaneous Test with Coccidioidin. Review of the Literature and Report of a Series in Texas.** *J. Lab. & Clin. Med.* 1946, Dec., v. 31, No. 12, 1317–24. [39 refs.]

"1. The literature pertinent to the cutaneous test with coccidioidin is reviewed.

"2. A report is made of a group of 413 subjects in Dallas, Texas, comprising nurses, medical students, and general hospital patients who were subjected to intracutaneous coccidioidin tests. In this group, an incidence of 2·66 per cent. positive reactors was encountered.

WILLETT, F. M. & OPPENHEIM, E. **Pulmonary Infiltrations with Associated Eosinophilia.** *Amer. J. Med. Sci.* 1946, Nov., v. 212, No. 5, 608–12. [20 refs.]

Report of two cases of coccidioidomycosis.

SASHIN, D., BROWN, G. N., LAFFER, N. C. & MCDOWELL, H. C, with the assistance of P. J. BOEING. **Disseminated Coccidioidomycosis localized in Bone.** *Amer. J. Med. Sci.* 1946, Nov., v. 212, No. 5, 565–73, 5 figs.

Report of two cases.

SWEIGERT, C. F., TURNER, J. W. & GILLESPIE, J. B. **Clinical and Roentgenologic Aspects of Coccidioidomycosis.** *Amer. J. Med. Sci.* 1946, Dec., v. 212, No. 6, 652–73, 11 figs. & 1 chart. [23 refs.]

A study of 277 patients.

HEAT STROKE AND ALLIED CONDITIONS.

Molnar, G. W., Towbin, E. J., Gosselin, R. E., Brown, A. H. & Adolph, E. F. **A Comparative Study of Water, Salt and Heat Exchanges of Men in Tropical and Desert Environments.** *Amer. J. Hyg.* 1946, Nov., v. 44, No. 3, 411–33, 18 figs. [15 refs.]

The effects of Californian desert and Florida tropical climates upon nude and clothed male subjects have been compared, by means of some of the data obtained in field tests undertaken with the object of ascertaining the water requirements of troops in warm climates. The prevailing temperatures at the Florida station were similar to those at Batavia and Singapore, while those at the Californian station were similar to those of the North African desert.

Heat stress was defined as the sum total of the physical environmental factors determining the flow of heat from the human body to the environment. Two possible methods of integrating these environmental factors, viz., (*a*) the effective temperature scale, and (*b*) the net gain of heat from the environment, were used. It was emphasized that effective temperature does not take radiation and insolation into account.

Physiological strain was also defined as the sum total of the physiological reactions to heat stress. At present there was only one integrative index for measuring physiological strain and that applied only to shade conditions (Robinson, Turrell, and Gerking, *Amer. J. Physiol.*, 1945, v. 143, 21.)

The results here described indicate that heat stress, assessed by the effective temperature scale and environmental heat gain, and physiological strain assessed by the Robinson index, were greater in the open desert than in an open tropical climate, and that the stress and strain in tropical jungle swamp and desert shade were about equal. For nude subjects, the heat stress was about 3·4 times greater in desert sunshine than in tropical sunshine; for clothed subjects the figure was 2·4.

Water and salt values were studied in clothed subjects only. The daily sweat loss was about 2·1 times greater in the desert than in the tropics, while the fluid intake was 1·8 times greater in the desert, but the urine volume was the same in both regions (about 0·9 litres per day). The average renal chloride excretion was the same in both environments. In the tropics there was no correlation between chloride excretion and sweat loss but in the desert the (negative) correlation coefficient was low but significant.

Further observations on six persons were made during a hike through a jungle swamp. Five of them, each carrying a 30 lb. pack, hacked their way through the difficult terrain while the sixth man remained at base making meteorological observations. The mean daily effective temperature was 79°F., which was tolerably comfortable for the resting men. The others were exhausted after three hours hiking, although they were only sweating at a rate of 0·4 litre per hour. The salt intake was about 26 grammes per 24 hours for all the men, but whereas the five hikers excreted 8·6 grammes per 24 hours the resting man excreted 13·8 grammes. Sweat output was determined as the difference between daily fluid intake and daily urine output.

Evaporative loss was studied in greater detail in another series of tests; about 1,400 observations being made on subjects stripped to the waist and on clothed subjects. The evaporative losses were measured with the men sitting and walking in the sun and in the shade, and the results for the tropical and desert climates were compared. Variations in relative humidity (40 to 80 per cent.), and wind speed (2 to 19 miles per hour), and in the rectal temperature and rate of heat production in the sitting subject, did not affect evaporative

loss. There was a good linear relation between evaporative loss on the one hand, and solar intensity, dry bulb temperature and rate of heat production of the walking man, on the other.

In sitting subjects, clothing reduced evaporative loss by about 100 grammes per hour, but when evaporative loss was compared with rates of oxygen consumption there was no significant difference between clothed and nude subjects walking in the sun. It was calculated that 72 per cent. of the heat produced by working was lost by evaporation of sweat in tropical sunshine. In the desert all the heat due to working was lost by evaporation.

While persons were exposed for 1 to 2 hours to varying conditions (80° to 104°F.) in a series of about 100 tests, heat exchanges were calculated. All the results showed that although many subjects were actually gaining heat from the environment by radiation and convection, the loss by evaporation was sufficient to keep the body temperature practically constant. At air temperatures greater than 90°F., clothing reduced the heat gain by 75 to 150 kilogramme-cals. per hour but at temperatures between 80° and 90°F., clothing had no appreciable effect.

Temperature gradients between the skin surface and the deeper tissues were measured, and the results are briefly discussed. *F. A. Chrenko.*

MISCELLANEOUS DISEASES.

GELFAND, M. **Jaundice in Acute and Severe Infections in the African.** *J. Trop. Med. & Hyg.* 1947, Jan., v. 50, No. 1, 15–18. [11 refs.]

ANNING, S. T. **The Aetiology of Desert Sore.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Dec., v. 40, No. 3, 313–30. [33 refs.]

[This is a stimulating article and will, doubtless, lead to further research.] The author has studied 63 cases of " desert sore " in Northern Iraq and presents the results of his personal investigations and reading of the literature. The condition—if it be a single pathological condition—has a wide geographical distribution, having been reported from South and East Africa, Libya, Egypt, Palestine, India, Syria, Iraq, Iran, Australia and elsewhere. Aetiological factors which have been named [would it not be more correct to say, have been suggested or guessed at?] are many : contact with animals, insect-bites; contagion, avitaminosis, diphtheria, exposure to the sun's rays. Occupation plays a part only in so far as it entails risk of trauma, for the primary lesion seems to be nearly always some small wound, abrasion, insect-bite or the like which does not heal in the usual way, but becomes indolent and perhaps surrounded by satellite vesicles or pustules. They always seem to appear on exposed parts. After rupture of the pustules, ulcers form and later crusts, and, on healing, thin papery scars are left which may again break down, especially if healing leads to itching and consequent scratching. The general health is, in most cases, not at all affected and lymphadenitis is unusual. The bacteriology is very varied, as would be expected if the failure to heal is due to secondary contamination.

Fifty-one cases in the author's series were studied bacteriologically and the commonest organisms were : streptococci in 30 ; next, *Staphylococcus albus* in 19, *Staph. aureus* in 17, unspecified staphylococci in 14 and Gram-positive diplococci in a like number. *C. diphtheriae* was found in one only. Syphilis plays no part. Variations in the blood count were negligible ; a few showed a moderate leucocytosis, but the majority were within normal limits, as regards

both red and white corpuscles. Nutritional deficiency would seem to play some part, for healing is accelerated by giving of vitamin A or C or both, though examination of the food taken showed that these, though not maximum or even optimum, were at the same time by no means minimum. Low protein or high fat content of the diet did not appear to play any part in aetiology in the author's cases. More research is needed on the possible dietetic factors in the aetiology of this condition.

[The abstracter, who saw many cases of Veldt Sore in the South African War, would like to add a note on his personal experiences there. He has not seen cases elsewhere. The author states: "While it is agreed by most observers that cutaneous diphtheritic sores only occur when faucial diphtheria is present and in parallel outbreaks. . . ." The earliest reference given by Dr. Anning to diphtheritic infection is that of CRAIG, in 1919. The abstracter saw his cases in 1901–2, isolated cases here and there among officers and men whose ulcers were slow to heal under the usual local applications. The appearance of neuritic paralysis suddenly in one of these patients, an officer, led to further bacterial examination and the finding of the Klebs-Loeffler bacillus. Local application of tampons soaked in antitoxin was rapidly followed by healing of the ulcer and the like happy results followed in other cases. There was certainly no parallel outbreak of faucial diphtheria at the time. This does not, of course, rule out the possibility of the diphtheria infection being secondary, but it goes far to show that the indolence and slowness to heal is due to this organism in certain cases and one is left pondering whether "desert sore" is a single condition—a small wound such as might occur to anyone anywhere at any time, becoming secondarily infected with a variety of organisms—or a group of conditions with differing aetiology in different countries.] *H. Harold Scott.*

LANDAU, H. D., Mme. **A Complement Fixation Test for the Diagnosis of Lymphogranuloma Inguinale.** *J. Path. & Bact.* 1946, July, v. 58, No. 3, 568–71.

SHARPE, D. S. **An Unusual Case of Intestinal Myiasis.** [Memoranda.] *Brit. Med. J.* 1947, Jan. 11, 54, 1 fig.

The beetle *Ptinus tectus*, together with its larva, is a common pest of dry food products, but has not previously been found living in man. The patient in this case suffered from diarrhoea and abdominal pains. Some blood was noticed in the stools, and also a number of living *Ptinus* grubs. The conditions cleared up after giving one ounce of liquid paraffin at night for seven days. It is suggested that the *Ptinus* eggs were ingested with the food and hatched in the alkaline portion of the gut, and that the larvae were able to survive and grow.
Kenneth Mellanby.

RIBBANDS, C. R. **Experiments with Leech Repellents.** *Ann. Trop. Med. & Parasit.* 1946, Dec., v. 40, Nos. 3/4, 314–19.

"Dimethylphthalate was proved to be a very effective and durable land-leech repellent. A dose at the rate of 4 c.cm. per square foot, applied to cloth in a band 1½ inches wide, was completely repellent, under favourable circumstances, for six days. A dose at the rate of 0·06 c.cm. per square foot was more than 60 per cent. effective immediately after similar application."

GENERAL PROTOZOOLOGY.

TALIAFERRO, W. H. **Populations of Blood-Dwelling Species.** Reprinted from *Amer. Naturalist.* 1941, Sept.–Oct., v. 75, 458–72, 7 figs. [18 refs.]

This short review of some of the factors which influence the relations between the parasite and its host in protozoal infections, is based on reviews and original work by various investigators, including the present author, published during the last twenty years and referred to in the list of 18 references [15 have been abstracted in this *Bulletin*].

The author selects malaria (*Plasmodium brasilianum* in spider monkeys) and trypanosomiasis (*T. rhodesiense* in the mouse and guineapig and *T. lewisi* in the rat) as illustrative examples. Asexual reproduction of *P. brasilianum* is synchronous and continuous ; on the average, 9·5 merozoites are produced by schizogony every 3 days, but at least 7 or 8 of them fail to develop fully, while at each crisis the rate of destruction exceeds that of reproduction. While the numbers of the parasites in the peripheral blood vary greatly, some measurement of the rate of reproduction can be made [see TALIAFERRO & CANNON, this *Bulletin*, 1937, v. 34, 622]. Before immunity develops, the macrophages probably remove only the dead and dying plasmodia, but when immunity has been acquired the phagocytes, probably assisted by antibodies such as opsonins, attack and kill the active parasites [see GINGRICH, this *Bulletin*, 1941, v. 38, 650 ; COGGESHALL, *ibid.*, 293].

In trypanosomiasis, multiplication of the trypanosomes may be continuous by geometrical progression up to the death of the host, as with *T. rhodesiense* in mice which normally do not produce antibodies, while the same infection in other hosts may be a relapsing one owing to repeated formation of antibodies and antigens. Though selection plays an important part in the formation of relapse strains, antigenic changes may occur in the trypanosomes as shown in a clone [single-cell infection] and the changes may persist through many asexual divisions in many host passages.

In the case of *T. lewisi* in the rat, an inhibiting antibody named ablastin [this *Bulletin*, 1924, v. 21, 423] is formed and prevents asexual division, while trypanocidal antibodies are also produced and lead to cure of the infection ; since multiplication is inhibited, relapses do not occur and the infection dies out.

Reference is made to the mathematical treatment of the subject of infections in whole host communities by ROSS and by LOTKA [this *Bulletin*, 1923, v. 20, 298]. *J. F. Corson.*

GENERAL ENTOMOLOGY.

WU, C. C., GHOSH, S. M., MCCLYMONT, A. G. & ROY, D. N. **A Preliminary Report on some Laboratory and Field Experiments to determine the relative Effectiveness of Pyrethrum, D.D.T. and Gammexane D919 as Insecticides and Larvicides.** *J. Malaria Inst. of India.* 1946, June, v. 6, No. 3, 285–95.

Comparisons of the insecticidal properties of pyrethrins (1 per cent. concentrate), DDT (? commercial) and crude Gammexane [probably 13 per cent. purity] were made with powder and kerosene dilutions. The following conclusions can be drawn from the experiments :—

(1) *Tests with the insecticides as dusts.*

Crude gammexane was more toxic to cockroaches and bed bugs at low concentrations (0·1 to 1 per cent.) than DDT or pyrethrins ; but at higher doses

(1 to 5 per cent.) the pyrethrins were more toxic. DDT was not only less toxic but considerably less rapid in action.

The crude gammexane was most toxic to anopheline and culicine mosquito larvae in laboratory tests when applied as a powder.

(2) *Tests with kerosene solutions.*

[The method of preparing the gammexane solution is a little suspect; it would favour a high *gamma* content.] Spray experiments against houseflies, mosquitoes and sandflies (*Phlebotomus*) were conducted in a modified Peet Grady chamber. A 1 per cent. pyrethrin spray was compared with 5 per cent. DDT and 5 per cent. crude gammexane. The effects were as follows :—

The mortalities after twenty-four hours were all high but the knockdown in ten minutes was only complete throughout with pyrethrum. The DDT and gammexane gave a poor knockdown of *Musca* spp. and *Armigeres obturans*.

Kerosene solutions used as a mosquito larvicide in the field were effective as follows :—

1 per cent. pyrethrins : 3–6 days (in open), 9–13 (in shade)
5 ,, DDT : 5–8 ,, ,, 14–20 ,,
5 ,, Crude Gammexane : 3–9 days (in open), 12–16 (in shade)

A residual spraying of a small dummy mattress with 5 per cent. DDT or crude Gammexane had a good residual effect against bed bugs for fifty days in both cases.

DDT and Gammexane sprays were effective against head lice but not against their eggs.

J. R. Busvine.

YATES, W. W. **Time required for *Aëdes vexans* and *A. lateralis* Larvae to obtain a Lethal Dose of several Larvicides.** *J. Econom. Entom.* 1946, Aug., v. 39, No. 4, 468–71, 1 fig.

Experiments were done with larvae which hatched in the laboratory from eggs collected in the field. Lots of twenty-five larvae were exposed to the insecticides for different periods ($\frac{1}{2}$ to 4 hr.) in small dishes containing tap water. Afterwards they were transferred to clean water for recovery. Various DDT preparations were compared with standard insecticides.

The following are approximate percentage kills forty-eight hours after a two-hour exposure :—

Pyrethrum emulsion (2 gall. per acre)	100 per cent.
3 per cent. oil emulsion (2 ,, ,,)	95 ,,
Diesel oil (2·5 ,, ,,)	90 ,,
Phenothiazine in solution (1 p.p.m.)	79 ,,
5 per cent. Paris Green dust (2 lb. per acre)	96 ,,
0·1 per cent. DDT dust (·02 lb. DDT per acre)	7 ,,
0·025 per cent. DDT suspension (·02 lb. DDT per acre) ...	86 ,,
0·05 ,, DDT emulsion (,, ,, ,,) ...	84 ,,
0·1 ,, DDT in diesel oil (,, ,, ,,) ...	85 ,,

It will be observed that the only notably inefficient DDT preparation was the DDT dust (diluted with talc from a 10 per cent. commercial dust). The other preparations of DDT were slightly slower in producing an effect but the kills were comparable with heavy doses of orthodox larvicides.

J. R. Busvine.

AZIZ, M. A. **A Simple Device for the Application of DDT Larvicide.** [Correspondence.] *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Dec., v. 40, No. 3, 353–4.

An adaptation of an ordinary flit-gun by extending the tubing and piston handle to about 3 feet.

MADDEN, A. H., LINDQUIST, A. W. & KNIPLING, E. F. **DDT applied from the Ground for Control of Mosquitoes.** *J. Econom. Entom.* 1946, Aug., v. 39, No. 4, 463–7.

Applications of insecticidal solutions were made by men walking across jungle areas in Florida infested with *Aëdes taeniorhynchus* and *A. sollicitans*. The sprayers used were (*a*) a capillary tube sprayer which gave a consistently fine spray mist (particles about 18μ average diameter); (*b*) a paint spray gum which gave fine particles (18μ diameter) at first but, as the air pressure declined, gave more and more coarse droplets; and (*c*) a mechanical sprayer (·055 inch jet and 136μ particles). The insecticide used was mainly DDT in kerosene or "No. 2 fuel oil". Solutions of 5–20 per cent. were used to give dosages of 6 gm. DDT per acre. The results of spraying were estimated by the numbers of mosquitoes coming to bite observers in one minute intervals before and one hour after treatment.

Results showed that the effectiveness of the sprayers were in the order mentioned, (*a*), (*b*), (*c*). The capillary sprayer, using a small quantity of fluid (30 ml. per acre) required to be applied in 20 ft. swathes for greatest efficiency. The spray gun gave good results with 40 ft. swathes using heavier liquid doses (120–250 cc. per acre). There is a need for a specially designed light, portable apparatus for applications of this kind. The kerosene or fuel oil alone had a considerable effect even without DDT when used at the rate of 125 cc. per acre or more.

Gammexane applied at 0·75 gm. per acre was rather less effective than DDT at 6·25 gm. per acre in a single experiment. *J. R. Busvine.*

ELMENDORF, J. E., Jr., MARUCCI, P. E., GRIFFIN, J. B., MEYER, S. L. & RYAN, G. S. **Longevity of Killing Effect of DDT for Mosquitoes contacting Screen Wire painted with DDT Solutions.** *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 663–85, 5 graphs & 1 fig.

Wire mesh (18 to the inch) was treated with DDT in various solvents at different rates (50, 100 and 200 mgm. per sq. foot), the applications being made with cotton swabs. The lethal effects of the deposits on the mosquitoes *Anopheles albimanus* and *Aëdes aegypti* were tested by short contacts with the wire, induced by interposing it between the mosquito in a tube and a forearm which the insect would then attempt to bite.

It was found that solvents such as acetone and kerosene, which dried within a few hours and left crystalline DDT, were of comparatively low toxicity. Several minutes' contact were required to give a complete kill twenty-four hours later. With non-volatile solvents, Dieselene, mineral oil and SAE # 30 and SAE # 50 [American Army issue oils] four "instantaneous" contacts were able to produce complete kill at first; and after weathering for some fifty days, about a minute's contact was required. These deposits could be "revitalized" by spraying with solvent alone.

Loss of toxicity was considerably greater if the wire was weathered outdoors instead of indoors and the deposit was more difficult to "revitalize".

J. R. Busvine.

CRISTOL, S. J., HALLER, H. L. & LINDQUIST, A. W. **Toxicity of DDT Isomers to some Insects affecting Man.** *Science.* 1946, Oct. 11, 343–4.

After some difficulty, isolation of o,o'-DDT (1-trichloro-2,2-bis(o-chlor-phenyl) ethane) has been accomplished and some insecticidal tests made in comparison with p,p'-DDT and the o,p' isomer.

As compared with p,p'-DDT, the o,o'-DDT isomer was found to be of very low toxicity to adults and fourth stage larvae of the mosquito *A. quadrimaculatus* and to the housefly and the body louse.

Although the o,p' isomer was ineffective against the adult mosquito and the housefly, it was fairly effective against the mosquito larvae. *J. R. Busvine.*

Odum, E. P. & Sumerford, W. T. **Comparative Toxicity of DDT and Four Analogues to Goldfish, Gambusia, and Culex Larvae.** *Science.* 1946, Nov. 22, 480–82, 1 fig.

Jones, H. A., Titus, H. A. & Oberg, M. W. **DDT Emulsion Concentrates.** *Soap.* New York. 1946, Dec., v. 22, No. 12, 155, 157, 165.

Gersdorff, W. A. & Barthel, W. F. **Determination of Pyrethrins Deterioration.** *Soap.* New York. 1946, Oct., v. 22, No. 10, 155, 157.

Samples of pyrethrins were kept under different conditions for 170 days and then tested for their toxicity to houseflies by the turntable method. It was found that none of the samples lost their power if stored in the dark at 2°C. but at room temperature in diffuse light, or at 40°C. in the dark, there were very great losses of toxicity with 100 per cent. pyrethrin concentrate and fair losses in a 20 per cent. commercial concentrate. These losses were inhibited by addition of hydroquinine (0·1 per cent.) or by dilution with odourless kerosene.

Concomitant with loss of toxicity was the development of sludgy material insoluble in dichlor-difluor-methane (Freon) and the presence of matter insoluble in Freon is a good guide to loss of toxicity. *J. R. Busvine.*

Jones, H. A., McCollough, G. T. & Morton, F. A. **Effect of Storage on Insect Repellents.** *Soap.* New York. 1946, Oct., v. 22, No. 10, 151, 153.

Samples of the two repellents known as 6-2-2 (60 per cent. dimethyl phthalate 20 per cent. " Rutgers 612 ", 20 per cent " Indalone ") and 80–20 (80 per cent. dimethyl phthalate, 20 per cent " Rutgers 612 ") were stored in different containers under various conditions of temperature and light. After eight months their repellent values were tested against *Aëdes aegypti* and *Anopheles quadrimaculatus* and compared with freshly prepared mixtures of the same materials, each pair of tests being performed on the arms of one subject. The results are shown in a table.

The only decrease in repellency (accompanied by a tendency to become opaque) was shown by the 6-2-2 mixture stored in metal cans at room temperature and at 60°C. No loss in repellency was shown by 6-2-2 stored at 60°C., or in sunlight in amber bottles or in pyrex flasks. The 80–20 mixture appeared to be little affected, though a loss in value was shown by a sample stored in pyrex flasks at 60°C., but this was possibly due to contamination from the rubber stopper or some other source. *H. S. Leeson.*

Block, S. S. **Insect Tests of Wire Screening Effectiveness.** *Amer. J. Pub. Health.* 1946, Nov., v. 36, No. 11, 1279–86, 4 figs.

——. **Tests of Screening Effectiveness against Insects.** *Science.* 1946, Nov. 8, 447.

The second paper is a summarized version of the first.

While testing the efficiency of screening of the following mesh sizes : 18×18, 16×16, 14×14, 18×16, 18×14, and 18×12, the special object of the investigation was to compare the efficiency of rectangular with the usual square mesh openings, especially screening having 18 warp (length) wires and 14 filler

(width) wires all of standard diameter, 0·011 inches, and the 16×16 mesh. The test insects were *Musca domestica*, *Culex quinquefasciatus*, *Anopheles quadrimaculatus* and *Aëdes aegypti*. Normal and undersized *Aëdes aegypti* were used and outdoor tests were made against small, light-attracted insects. The experimental methods are described and the results tabulated and graphed.

Only normal sized and to a greater extent undersized *Aëd. aegypti* were able to pass through the 18×14 and the 16×16 meshes. This applied equally to both sexes and seemed to be related to the diagonal dimensions of the openings. It was found that there was no significant difference in the percentage escape whether the 18×14 screening was erected with the openings vertically or horizontally, but with 18×12 mesh the difference was in favour of the vertical position.

A mesh of 18×18 gave better protection than the 16×16 mesh against the undersized *Aëdes aegypti* and against *Aëdes taeniorhynchus* and the small, outdoor, light-attracted insects. *H. S. Leeson.*

LAURANS, R. Note sur l'action toxique du sulfure de polychlorocyclane à l'égard des aphaniptères. [**The Toxic Action of Polychlorocyclane Sulphide on Fleas.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 7/8, 295–9.

This compound, which is apparently formed by two molecules of chlorinated benzene united by a sulphur atom, is said to be chemically stable and fairly persistent. On the basis of some rather crude tests, it appears to be effective against fleas when used as a 4·5 per cent. dust. Its action is slightly more rapid than that of DDT. *J. R. Busvine.*

COLE, L. C. & KOEPKE, Jean A. **A Study of Rodent Ectoparasites in Mobile, Ala.** *Pub. Health Rep.* Wash. 1946, Oct. 11, v. 61, No. 41, 1469–87, 1 fig. [40 refs.]

The authors are interested in the ectoparasites of domestic rats, in relation to the epidemiology of plague and murine typhus: it will be remembered that there is some evidence incriminating a mite (*Liponyssus bacoti*) as well as *Xenopsylla cheopis*.

The work has been done at Mobile, a small port in Alabama, U.S.A. The authors examined rodents trapped alive through the year 1934. They had nearly 6,000 *Rattus norvegicus*, and a couple of hundred *R. rattus* and house mice. Every rat was searched for fleas, and every tenth one also for mites and lice.

Among over 45,000 fleas, 64 per cent. were *X. cheopis*, and over 16 per cent. *Echidnophaga gallinacea*. Among about 2,600 mites two-thirds were *Laelaps hawaiiensis*: *Liponyssus bacoti* was rare, just over 1 per cent. of mites. Of lice, *Polyplax spinulosa* made over 60 per cent., species of *Hoplopleura* the remainder.

The authors discuss the method of dealing with exceptionally high counts of a flea or other parasite on an individual rodent: such a count raises the arithmetic mean. They follow RUMREICH and WYNN (*Pub. Health Rep.*, 1945, v. 60, 885) in limiting all "counts to a particular value, determined by fitting a curve to the frequency distribution" (the method not being further explained). They arrive at 40 as the limit for *X. cheopis* in Mobile, and all higher counts are recorded as 40: other limits are used for other parasites, and we gather that some other limit might be used for *X. cheopis* in a different place. In fact the "index", after being handled in this rather rough and empirical way, loses its great value of being able to be compared for different places. [Other and surely more reputable ways exist for dealing with exactly this problem, if one is not content with the arithmetical mean.]

The incidence of the five commonest sorts of flea is tabulated monthly: for both sorts of rat for the year, 67 per cent. of all *R. norvegicus* were infested with *X. cheopis* and the year's mean (*i.e.* the "cheopis index" in the generally accepted sense) was 5·22. The figure was lowest in February and March, highest in July. On the year as a whole, the commercial part of the town had a higher *cheopis* index than the residential, or the water front. Food shops had a higher index than other buildings.

The paper contains many other tables, and a consideration of the relation of ectoparasite to particular localities in the town. *P. A. Buxton.*

JONES, B. **Impregnating Polyvinyl Alcohol with Picric Acid for the Simultaneous Staining and Permanent Mounting of Acarina.** *Proc. Roy. Entom. Soc. London.* 1946, Dec. 16, v. 21, Pts. 10/12, 85–6.

The author has experimented with polyvinyl alcohol (a valuable new mounting medium, particularly suitable for small insects and mites). He has added picric acid to the formula, which stains very delicate chitinous structures. His formula for a permanent mountant is as follows:—

"Solution. 6·3 gm. polyvinyl alcohol, 18 cc. absolute alcohol saturated with picric acid, 35 cc. distilled water, 45 cc. lactophenol.

"Method. 1. 6·3 gm. of the polyvinyl alcohol are transferred to a clean dry beaker flask (approx. 250 cc. capacity). 2. Add 18 cc. of absolute alcohol which is first saturated with picric acid. 3. Stir thoroughly with a glass rod to form a homogeneous paste. 4. Add 35 cc. of distilled water. 5. Stir thoroughly to a gelatinous consistency. 6. Add 45 cc. of lactophenol. 7. Heat the solution in a water-bath until it clears and then leave to cool."

In this (and in a simple "temporary mountant") small insects, etc., can be mounted straight from life, or from water or alcohol. The material stains the chitin in twenty-four hours, and becomes hard in forty-eight hours.

[There is no doubt that polyvinyl alcohol is of great value. The author by no means exhausts the list of its valuable qualities. It is far from certain that supplies of an appropriate grade will continue to be manufactured in any part of the world.] *P. A. Buxton.*

DE MEILLON, B. **Effect on some Blood-Sucking Arthropods of "Gammexane" when fed to a Rabbit.** [Correspondence.] *Nature.* 1946, Dec. 7, 839.

The author finds that if Gammexane is given by mouth to the rabbit, the animal's blood is toxic, even lethal, to certain blood-sucking insects.

He has used the pure gamma isomer of hexachlorocyclohexane. He has mixed this substance, a powdered solid, with agar and water, which set solid when cold. In this way he has given doses of about 50 mgm. of insecticide, by the mouth, to rabbits. He generally worked with rabbits which had received some four or five doses (presumably on successive days).

Bed bugs (*Cimex lectularius*) feed readily on such a rabbit and a mortality of about 50 per cent. of nymphs occurs after a single meal; but adult bugs suffer a temporary paralysis, recover and are able to lay eggs. All *Aëdes aegypti* which feed die. *Ornithodorus moubata* attach normally but take a very small meal, after which they detach themselves and show inco-ordination: some die.

P. A. Buxton.

LABORATORY PROCEDURES.

BAROODY, B. J. **Modification of the Faust Method in the Detection of Cysts and Ova.** *J. Lab. & Clin. Med.* 1946, Dec., v. 31, No. 12, 1372–4.

In 1945 the author had occasion to examine ever-increasing numbers of troops arriving from the Pacific theatre of operations and suffering from amoebiasis. In his experience the Faust zinc sulphate flotation method had proved most satisfactory for the detection of amoebic cysts; nevertheless, in many cases, even with this method persistently negative results were found after prolonged and repeated examinations, even after purgation.

Believing that in Faust's routine method the stool sample might be too small, the author modified it by combining it with his own technique for detecting schistosome ova [this *Bulletin*, 1947, v. 44, 333].

The modified method consisted essentially of the following steps :—

1. Ten gm. of faeces are placed in a 125 cc. stoppered Erlenmeyer flask containing about 75 cc. of warm water (about 40°C.), and shaken until emulsified.

2. The emulsion is strained through a layer of wet gauze into a 50 cc. centrifuge tube, and centrifuged at 2,500 r.p.m. for 1 minute. The supernatant fluid is discarded, and warm water added from a regulated tap (to disperse and cleanse the particles). Centrifugation and washing are repeated once more, and the supernatant fluid is finally discarded.

3. About 10 cc. of warm water are added and the sediment agitated by shaking, after which all the contents are poured quickly into a 15 cc. centrifuge tube and centrifuged for 1 minute at 2,500 r.p.m. The supernatant is decanted.

4. About 10 cc. of zinc sulphate solution (33 per cent. and S.G.1.180) are added to the sediment and stirred. Zinc sulphate is added nearly to the top of the tube, which is centrifuged for 1 minute at 2,500 r.p.m. Ova and cysts will float to the surface.

This technique differs from Faust's original method in three particular respects :—

(1) The chances of detection in lightly infested cases are increased by the use of a much larger sample of faeces.

(2) The use of warm water eliminates a great deal of the scum or fats, which otherwise remain with the sediment and tend to float when zinc sulphate is added, thus obscuring the eventual microscopical preparation.

(3) The initial use of a 50 cc. centrifuge tube provides for receiving a large sample of the original 50 gm. of faeces; also the proportion of sediment to the size of the tube decreases the number of washings and centrifugations required to arrive at a clear supernatant fluid—3 or 4 such washings are usually adequate.

H. J. O'D. Burke-Gaffney.

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

KAUNTZE, W. H. **The Occurrence and Control of Transmissible Diseases in British Colonial Territories from the Outbreak of the Recent War to December, 1945.** *Bull. Office Internat. d'Hyg. Publique.* 1946, Apr.–May–June, v. 38, Nos. 4, 5 & 6, 281–6.

Dr. KAUNTZE discusses this problem under three main heads: (1) general epidemiological control arrangements; (2) research; and (3) communicable diseases 1939 to 1945.

Under the first heading he outlines the temporary arrangements which became necessary, owing to the interruption by war of relations with the *Office International d'Hygiène Publique*, to maintain the exchange of epidemiological information and the co-ordination of control measures within the Colonial Empire and in relation to foreign territories.

Reference is made to the suspension by the Egyptian Government in 1941 of the Regional Bureau at Alexandria, and its temporary replacement by an exchange service, with the Quarantine Directorate in Alexandria as a centre ; to the International Sanitary Convention and that for Aerial Navigation, in 1944, and the assumption by UNRRA of the rôle of the *Office International d'Hygiène Publique* as a centre for the collection of Colonial epidemiological information ; to the establishment in 1941 of the Inter-Departmental Committee on Yellow Fever Control ; and to the Trinidad Conference in 1943, which considered the formation of a model Quarantine Ordinance for adoption by the British West Indian Governments in order to co-ordinate quarantine procedure.

Operational and transport problems met with by His Majesty's Forces called forth much investigation relating to the control of infectious diseases, and valuable knowledge was obtained. The research measures inaugurated are discussed under the second heading.

The Colonial Medical Research Committee was re-established in 1945, and since then a Malaria Sub-Committee has been set up, to consider co-ordination of malaria research in the British African Colonies. A similar Committee, concerned with Tsetse and Trypanosomiasis research and control was established in 1944.

The specific investigations carried out during the period under review are outlined, the principal work being : (1) the mosquito research by the British Guiana Malaria Research Service, which incriminated *A. darlingi* as the only carrier species of practical importance and which showed that control measures with insecticides like DDT may solve the malaria and filaria problems in that territory ; (2) Dr. Blacklock's investigations into the high rate of malaria incidence in passengers and crews of ships arriving from West Africa, and the improvements obtained in Freetown as a result of his recommendations ; (3) Dr. Muirhead Thompson's studies of *A. gambiae* in West Africa ; (4) Mr. Symes' extensive inspections of, and recommendations regarding yellow fever control in aerodromes along the main air routes in Africa, and his field researches, with a special team in East Africa, into the use of various insecticides ; and (5) Dr. Lewthwaite's enquiry into scrub typhus in the Far Eastern theatre, which resulted in his recommendation of the use of dibutyl-phthalate as a mite-repellent, the employment of the " Fulton " cotton-rat vaccine, and the establishment of a Scrub Typhus Research Laboratory.

Under the final heading Dr. Kauntze discusses the incidence of six prominent infectious diseases in the Colonies, and points out that despite the large movements of men all over the world and the increased rapidity of air travel, no serious pandemic of one of the formidable epidemic diseases occurred in British Colonial Territory during the period under review—a striking tribute to the efficiency of the temporary arrangements made.

Yellow Fever control encountered many difficulties during the war, and the need for it was emphasized by the severe outbreak of that disease in the Anglo-Egyptian Sudan in 1940–1, and by the findings of the Yellow Fever Research Institute in Entebbe. An Inter-Departmental Committee was set up in 1941, and representation included Service and Civil Departments, and the Governments of the Union of South Africa and Southern Rhodesia.

Sporadic outbreaks of yellow fever occurred in a number of places in the West African Colonies, and the first cases in East Africa consisted of one each from Uganda in 1941 and Kenya in 1942. Mass inoculations were undertaken.

Plague was reported in 1941 in Uganda (168 cases, 164 deaths); in Kenya (92 cases, 37 deaths); and in Palestine (7 cases). In 1945, 60 cases, with 19 deaths, occurred in Malta. Appropriate measures were taken, including a visit by a specialist in anti-rodent measures from England.

Smallpox occurred in Gibraltar in 1944 (20–30 cases); Kenya, 1945 (91 cases, 9 deaths); Ceylon, 1945–6 (194 cases, 37 deaths); and in varying degrees of severity in West Africa from 1939 to 1945.

The most severe outbreaks of *poliomyelitis* were: (1) in Malta (1942–3). There were 483 cases. A special report was made by Professor Seddon. Another outbreak occurred in 1945–6, with 80 cases up to March 1946; (2) in Mauritius (1945) where there were 872 cases, 58 being fatal; (3) in St. Helena (1945–6), involving 214 cases, of which 11 were fatal; (4) and Singapore (1945–6) where there were about 85 cases.

Cerebrospinal meningitis was epidemic in E. Africa in 1941. In the same year, outbreaks occurred in Nigeria and the Gambia, and in 1945 there was an epidemic in the Gold Coast, and again in the Gambia. The incidence was as follows:—

		No. of cases	Deaths
East Africa (1941)	Tanganyika	721	171
	Kenya	164	46
	Nyasaland	168	48
	Uganda	36	8
West Africa	Gold Coast (1945) ...	9,863	1,056
	Nigeria (1941) ...	115	48
	Gambia (1941) ...	29	9
	,, (1945) ...	9	3

In Kenya, around Mombasa, an epidemic of *relapsing fever*, believed to be louse-borne, began in November 1945. At the end of the year, there had been 1,596 cases, with 377 deaths. DDT was used on a considerable scale as a delousing agent.

Louse-borne *typhus* occurred in the Aden Protectorate in 1943–44, and is believed to have been introduced by Jewish refugees.

[This note is a remarkable tribute to the manner in which international co-operation and control of transmissible disease in the British Colonial Territories was maintained throughout the War despite the enormous difficulties of communication, staff and funds and the transport and troop movements involved.] *H. J. O'D. Burke-Gaffney.*

SAPERO, J. J. **Tropical Diseases in Veterans of World War II.** *New England J. of Med.* 1946, Dec. 12, v. 235, No. 24, 843–6.

Discussion of tropical diseases occurring among some 10 million U.S. Servicemen who had served overseas between 1942–1945, including incidence figures.

BOOK REVIEWS.

VAN DEN ENDE, M., STUART-HARRIS, C. H., FULTON, F. & NIVEN, J. S. F., with C. H. ANDREWES, A. M. BEGG, W. J. ELFORD, M. H. GLEESON WHITE, W. L. HAWLEY, K. C. MILLS, F. HAMILTON & C. C. THOMAS. **Chemotherapeutic and other Studies of Typhus.** *Med. Res. Council Spec. Rep. Ser. No. 255.* 246 pp., numerous figs., charts & pls. 1946. London: H.M. Stationery Office. [12*s.* 6*d.*]

This report is rightly described in the preface as a "substantial monograph" in which "are recorded the results of clinical and laboratory studies

of typhus fever." The title of the volume may convey a misleading impression by suggesting that the authors deal chiefly with the chemotherapeutic aspects of the disease. It is true that the original purpose of the studies was to test the effectiveness of two drugs in the treatment of human typhus, but apart altogether from the melancholy interest of this part of the investigation the book is a very important contribution to knowledge of the disease; it will, indeed, take its place among the classical works on the subject, such as those by MURCHISON, and by WOLBACH, TODD and PALFREY.

The experimental work leading up to the present trials has already been fully described [see this *Bulletin*, 1945, v. 42, 20]. Among 238 substances tested on infected mice two gave special promise of success when administration was begun within 42 hours of the infecting inoculation. These drugs were *p*-Sulphonamidobenzamidine hydrochloride (V147) and *p*-Sulphonamidobenzamidoxime hydrochloride (V186). Apart from 11 other substances which were somewhat effective all the remaining drugs were found ineffective, including *p*-Aminobenzoic acid (PABA) which has since been very favourably reported on by a number of competent observers. The present authors state in a footnote that PABA has been found by them to show " a little activity " when given by the mouth.

Full details are given of the trials of V186 and V147 in North Africa and Naples; unfortunately very few cases were available for treatment within the first few days of the illness, but in the conditions in which the tests were carried out it appeared that the drugs caused no obvious benefit, and toxic effects were observed in many cases.

In the first chapter, of four pages, ANDREWES, BEGG, and VAN DEN ENDE describe a series of experiments by which the toxicity of the two drugs was determined. The maximum tolerated daily doses, by the mouth, of both drugs, in gm. per kgm. body weight, were 2·0 for mice and 0·3 for guineapigs; the doses of V186, which alone was tested in these cases, were 0·25 gm. for rhesus monkeys and at least 0·13 gm. for human volunteers.

The great tolerance of mice is a striking feature of the tests.

The second chapter runs to 118 pages; all the authors of the report except Andrewes, Elford and Mills, shared in its production.

Preliminary trials of V186 were made in Algiers between July and September 1943; these showed clearly that no obvious clinical effect could be expected when the drug was given from the second week onwards; in seven of the nine treated patients the first dose was given on the 10th day or later. Kidney damage was thought to have been caused or aggravated in one case.

The main part of the trial was carried out during the Naples epidemic; 30 patients were treated—27 with V186 and three with V147. There were 30 comparable control patients who, like the treated, belonged to the over-15 age group. Full details are given of the clinical and pathological findings in all the above patients and also in other cases not forming part of the critical tests. In 10 cases, treatment began between the 4th and 6th day; in 9 between the 7th and 10th day, in 11 cases the day of onset was not known.

The fatality rate was higher in the treated group; three of the 25 patients who were under 40 died, and four of the five over 40; in the control group, the corresponding figures were one among 21 and four among 9. No significant differences were observed in the duration of the fever after admission or in the total duration of the illness. Among the patients adequately treated from the 6th day or earlier the average duration of the fever was 11·7 days whereas among those treated from the 7th day or later the average was 14 days: the authors suggest that if still earlier treatment could have been instituted the infection might have been aborted.

The toxic effects recorded were : vomiting in 12 of the treated and in only three of the controls ; a shock-like state in five of the treated, and kidney damage manifested by uraemia and post-mortem findings in at least three cases ; this damage was believed to have been caused or aggravated by the drug.

The clinical features of the disease were closely studied both in the treated and control cases. From an analysis of the findings in 50 representative untreated patients the following list has been prepared ; the figures refer to percentage incidence. The fever was remittent in 32, continued in 26, continued at first and later remittent in 18, and irregular in 20. Tachycardia occurred in 90 ; increased respiration rate in 80 ; obvious dehydration at some time in 58 ; flushed face in 52 ; conjunctival injection in 54 ; a macular or haemorrhagic rash in 94 ; gland enlargement in 50 ; bronchitis or bronchiolitis in 58 ; low blood pressure in 74 ; splenomegaly in 42 ; albuminuria in 46 ; mental symptoms in 68 ; meningism in 20 ; incontinence of urine, in females in 100, and in males in 50 ; and peripheral gangrene in 10.

Rickettsiae were isolated from 17 of the 19 patients from whom samples of blood were taken for animal inoculation ; altogether 22 such samples were taken and the usual procedure was to inject 5·0 cc. of whole blood intraperitoneally into a guineapig. The strains used for transfer to mouse lungs in the form of guineapig-brain suspensions were taken at the 4th to the 6th guineapig passage ; all the 11 strains employed were found to be well adapted for initiating a series of lung passages.

Repeated serological tests were carried out in 59 cases in which the date of onset was known. Curves are reproduced to show the rise in titre observed in the agglutination reactions. The *Proteus OX19* and epidemic rickettsial titres showed rapid rises, reaching, on the average, significant diagnostic levels of 1–200 and 1–25 respectively before the end of the first week of the illness. *Pr. OX2* and murine rickettsiae were also agglutinated at rising titres, but the levels reached were much lower.

The rickettsia-agglutination tests had the advantage of showing diagnostic differences between epidemic and murine typhus ; the antigens employed were prepared by the Fulton and Begg method [see the part of this abstract dealing with chapter 4]. A tendency to " zoning " had to be guarded against by using a large series of dilutions.

A slide-agglutination test in which methylene-blue-stained *Proteus OX19* was used, is described as useful and convenient.

Complement-fixation tests, in which fresh Fulton and Begg antigens were used, gave highly specific responses with epidemic and murine sera. After storage the antigens yielded higher, but less specific, titres.

The blood changes among the patients of the treated and control groups were closely studied ; no significant differences were observed between the two. No striking or characteristic changes were found in the blood-cell counts ; the leucocyte counts showed a wide range of variation but on the average they were lower than normal.

The blood urea was raised in most of the severe attacks ; in 13 out of 18 " grave " cases the level rose above 100 mgm. per 100 cc. and 10 of the 13 patients died, whereas among the remaining five patients only one died. Only four among 20 " moderately severe " cases yielded levels above 100 mgm. and none of these was fatal. Among 11 mild cases, the 100 mgm. level was never reached. Azotaemia was usually accompanied by oliguria or anuria. Urinary output was often greatly reduced in severe and fatal cases. Albuminuria was usually slight ; urea clearance was often, but not always, greatly reduced in the severest cases.

The post-mortem findings are described in detail and are illustrated by 24 good reproductions of photomicrographs. Special emphasis is laid on the severity of the lesions sometimes observed in the heart and kidneys. The conjunctiva is said to be the most reliable tissue for use in detecting the vascular lesions. Proliferative changes in the small arterioles were more striking than necroses.

In the 3rd chapter, VAN DEN ENDE and MILLS describe experiments which they regard as showing that the pulmonary titration method of estimating potency of antirickettsial sera may be helpful in testing vaccines and antisera. The method is based on the observation that when mice are inoculated intranasally with rickettsial suspensions the number of focal lesions produced in the lungs is reduced when antisera are mixed with the suspensions [see this *Bulletin*, 1945, v. 42, 20]. Quantitative results were obtained when the antisera were of high potency.

In the 4th chapter, FULTON, VAN DEN ENDE, ELFORD, and MILLS, describe the results of various tests of the potency of murine-typhus vaccines prepared in four different ways—(*a* and *b*) from yolk-sac cultures purified by Craigie's method and in the crude form (*c* and *d*) from infected mouse lungs in the crude form or after purification by Fulton and Begg's kieselguhr method in which triturated lung suspensions are differentially centrifuged and further purified by the addition of a suspension of kieselguhr by which tissue particles are carried down leaving an almost pure suspension of rickettsiae. Details of the method are given.

When vaccines were prepared so that they contained approximately equal numbers of rickettsiae, no significant difference was found in the potency of the four vaccines. It was assumed that the so-called soluble antigen contained in Craigie's vaccine could not have a great immunizing value. Yolk-sac vaccines had the great advantage of high yield; one yolk sac supplied nine times as much vaccine as one mouse lung.

The most reliable and convenient method of testing vaccines was considered to be the estimation of their power to protect mice against the "toxicity" of rickettsiae injected intravenously.

In the 5th chapter, FULTON and BEGG deal with the antigenic structure of epidemic and murine rickettsiae; they describe a large series of agglutination and complement-fixation tests, on the basis of which a very interesting hypothesis is proposed. Two propositions are stated:—(1) "Antibodies formed in response to one antigen, although adjusted to a certain structure, are not entirely uniform, but vary in specificity to some extent," and (2) "The heating of some antigens to 100°C. creates a new specificity." In this connexion it is also assumed that "a labile antigen may be degraded *in vivo* and give rise to antibodies not only to its native form but also to those degradation products which are antigenic."

The authors' hypothesis differs from the one generally accepted in that the heat-labile antigens are regarded as highly complex, giving rise in the body to the production of antibodies which are not type-specific as well as to those which are type-specific; the former being produced in response to the action of such heat-labile antigens as have become degraded *in vivo*.

The hypothesis is somewhat complicated, but not more so than the antigenic structure of the rickettsiae; it will be studied with keen interest by serologists; its chief practical bearing is that in serum tests for differentiating epidemic and murine typhus "it is essential to confine attention to that fraction of antibodies, in each immune serum, which is highly specific," and therefore to use freshly prepared antigens which have not been degraded by heat or chemicals.

In the opinion of the authors " the differences between the murine and epidemic strains are sufficient to justify according each specific status."

[A view which seems to have something in common with the present hypothesis was stated by SHEPARD in 1944 (see this *Bulletin*, 1946, v. 43, 21). This worker produced evidence that the cross-immunity between epidemic and murine typhus was not associated with the heat-stable antigens but was due to " a similarity of the unheated antigens."]

Appendix A contains summarized reports of 13 representative cases, including six controls and five treated with V186.

Appendix B consists of a list of the 238 drugs tested for activity in the treatment of experimental typhus in mice. *John W. D. Megaw.*

AUSTRALIA, COMMONWEALTH OF : DEPT. OF HEALTH. SERVICE PUBLICATION (SCHOOL OF PUBLIC HEALTH AND TROPICAL MEDICINE). No. 6. **Spiders, Ticks and Mites, including the Species Harmful to Man in Australia and New Guinea. Section 1. Descriptive** [TAYLOR, F. H., F.R.E.S., F.Z.S.]. **Section 2. Clinical** [MURRAY, R. E., M.B., B.Sc., D.T.M. (Sydney)]. 275 pp., 184 figs. & 1 pl. 1946, Sept. Glebe, New South Wales : Australasian Medical Publishing Company Ltd.

This book is a technical compilation on venomous spiders, mites and ticks of Australia and New Guinea. Considerable parts of the text and nearly all the figures are from other sources, which are acknowledged. It is addressed to the " man on the land, the medical practitioner and the public in general." We have formed an opinion that in Australia the members of these classes must have an insatiable thirst for the finer points of anatomy of the Acarina.

The first part of the book deals in a systematic way with these organisms. The author of this section starts with the spiders, defining sub-families, genera and species of those which are venomous (*Atrax* and *Latrodectus*). He has also taken considerable trouble to explain technical terms and to illustrate them.

The account of the Acarina occupies over two hundred pages with about 180 line drawings. The author has delimited the field widely, but somewhat irregularly. For instance, in dealing with the ticks he includes all those which occur in Australia. Among them are one or two which have a minor importance to man himself and several which are important parasites of domestic animals : others which are included feed only on sea-birds, swallows, reptiles, marsupials and so forth. But when he reaches the mites, the author takes a much more restricted view, limiting himself to those which attack man and making no reference even to the species which cause mange and such conditions in domestic animals. One notices for instance that the account of *Sarcoptes* deals only with these mites as they occur on human beings, without a passing reference to the very closely related forms on animals or to the possibility that man may be infested from animals. Indeed it must be stated that the parasitology of scabies is not dealt with in a satisfactory way for it contains references to old papers which are out of date, but almost no reference to the work of K. MELLANBY, for the curious reason that his book is generally available. The account of the mite which causes crusted scabies could only be described as uncritical and archaic.

The Trombiculidae are dealt with in an inclusive way and this is perhaps wise, for it would be difficult at the moment to define those which directly affect human beings. We feel, however, that a little more selection might have been used : it seems excessive to give thirty pages and many figures to *Neoschöngastia*, no species of which is known to attack man. A colleague more expert than myself finds many points to criticize. It is stated erroneously (p. 150) that the larvae of the genus *Trombicula* are yellowish : some of them

are vermilion. The author states that he has constructed a figure and a table of measurements of *Schöngastia vandersandei* of Oudemans: in doing this he took unnecessary trouble, for Oudemans has published excellent figures and descriptions in his paper. The author has not decided whether a particular genus should be referred to as *Leeuwenhoekia* or *Acomatacarus*: it appears under one name in the key and the other in the descriptions. Moreover under the hosts of *L. australiensis* no species are recorded except the casawary and "? *Isoodon*": but it is stated in the text that this species attacks man severely in the neighbourhood of Sydney. The text is open to criticism in a number of other technical points.

The second section of the book, which runs to thirty pages, deals with the medical and pathological effects of the bites and infections due to the Acarina. It contains a considerable and useful collection of clinical notes on tick paralysis, bites of venomous spiders and of the tick *Ornithodorus gurneyi*. It is, we feel, characteristic of the book that on so disputed a subject as tick paralysis the authors give us excerpts but no summary. There is a section on irritation of the skin due to a great variety of mites, *Sarcoptes*, *Tyroglyphus*, *Pediculoides*, *Liponyssus*, *Trombicula* and others. The view is accepted that copra itch is due to *Tyroglyphus*: it may be doubted whether this is proved and one is not convinced that what Castellani wrote in 1912 is the last word in the matter. It is curious to see that much more space is given to the occurrence of mites in the lung than to the relation of *Trombicula*, etc., to scrub typhus. The latter subject, of immediate interest to Australia, is passed over in half a page of not well-selected information. Admittedly it would have been no easy matter to write the subject up just at the moment when the present manuscript went to press: but surely it was an essential part of the task of compilation. We can find no reference to Q fever, a distinctive Australian disease, carried by ticks.

Much of the information which has been collected and put into this book is familiar and comes from all over the world. When one looks for Australian data, the result is disappointing. For instance, one can find nothing about the importance of *Sarcoptes* or *Pediculoides* as parasites of man in Australia, and nothing about the distribution of the common ticks of domestic animals in that continent.

The details given about the species of hosts often leave questions unanswered, for instance: "*Ovis aries* Linn: men's boots in ti-tree camp." "*Homo sapiens* L.; Kingfisher, gen. et sp." "? Found on boots in kunai grass."

The authors give nearly all the names of species of hosts in Latin. One may suppose that the reader would be familiar with *Homo sapiens*, *Bos taurus*, and *Equus caballus*, and might even be able to identify *Varanus*, *Macropus*, or *Passer domesticus*: but we doubt whether the medical reader (here referred to as a "medico") could identify *Phascolomys*, *Diomedea*, *Aptenodytes*, *Echymipera*, *Lygosoma*: as there is nothing to indicate which is a mammal, bird or reptile, it might even be difficult for him to know where to look up these names.

P. A. Buxton.

DOGIEL, V. A. [Professor of Zoology in the University of Leningrad.] **Textbook of General Parasitology.** Published by the People's Commissariat of Education of R.S.F.S.R., Leningrad. 1941, 297 pp. 219 text figs. [7 Roubles.]

The great majority of modern text-books of parasitology deal almost exclusively with parasitic animals of economic importance in medical and veterinary sciences, while the general principles of parasitology are usually disposed of in a relatively brief and inadequate introduction to the systematic account of the parasites. Though such text-books provide the student with

concrete information required for the identification and diagnosis of the parasites and for an understanding of the host-parasite relationships, they lack a sound theoretical background of comparative knowledge of the phenomena connected with parasitism in general. Generalizations based on studies of entozoic relations throughout the animal kingdom are of great importance in applied parasitology, for they provide valuable material for the interpretation of the existing data, and serve both to throw light on newly discovered facts and to direct investigations along promising paths. General parasitology stands in the same relation to applied parasitology as comparative anatomy to systematic zoology. Some of the problems with which it deals, such as morphological and physiological adaptations in parasites, their ecological requirements and host-parasite relationships are of fundamental importance in biology.

The book under consideration, which Prof. Dogiel defines as a treatise on the *general biology of parasites*, fulfils all these tasks and is intended to serve as an introduction to applied parasitology. In accordance with this plan, the sections into which it is divided are devoted to various biological phenomena connected with parasitism, the examples being selected from diverse groups of parasites irrespective of their systematic position, provided they serve to illustrate the same phenomenon.

The first part of the book is devoted to parasitism in general and to a characterization of parasites and their life-cycles. The author first discusses the concept of parasitism and arrives at a definition of parasites, as " organisms which utilize other living organisms as a source of food and habitat." He further considers the various forms of entozoic relations, which are divided into synoecia (including commensalism), symbiosis and parasitism proper, the prevalence of parasitism in the animal world and its origin. Other chapters deal with the method of invasion of the host, morphological adaptations of parasites to their mode of existence and their life-cycles, including alternation of generations of parasites and hosts.

In the second part, an account is given of the effect of the external environment on the parasite fauna of the host, a subject in which much of the pioneer work has been carried out by the author and his school. The influence of the age, food, mode of life and migrations of the host upon its parasites as well as the influence upon them of zoogeographical factors, are discussed in detail. The final chapter in this section is devoted to " complex " ecological and parasitological investigations of ectoparasites.

The third and last part deals with the host-parasite relationships, *viz.* specificity of parasites, the effect of parasites upon the host and *vice versa*, while in the last chapter the author discusses the economic importance of parasites, in medicine, veterinary practice and agriculture.

The book is illustrated by well-selected figures and diagrams—many of them original—and is provided with references to literature and an alphabetical index of Latin names.

In this review it is only possible to give a brief outline of the contents of this treatise, which is an outstanding contribution to the parasitological literature, unique in conception and masterly in presentation. There can be no doubt that the author has fully and admirably achieved the object he had in view. This valuable work will be indispensable to all serious students and research workers in parasitology as well as to biologists in general, and Russian readers are fortunate to have it at their disposal. It is to be hoped that it will be made available to foreign readers as well. *C. A. Hoare.*

Printed under the authority of His Majesty's Stationery Office
By The South Essex Recorders, Ltd., Ilford.

(116) Wt. P11/325 5/47 S.E.R. Ltd. Gp. 432

ALPHABETICAL LIST OF AUTHORS OR SOURCES.

Adler, S. & Tchernomoretz, I., 408.
Alfonso Armenteros, J., 459.
Anigstein, L. & Whitney, D. M., 412.
Anning, S. T., 462.
Australia, Commonwealth of, 476.
Avery, J. L., 445.
Aziz, M. A., 465.

Ball, E. G., 400.
Banerjee, S. & Ghosh, N. C., 452.
Bang, F. B. & Hairston, N. G., 435.
——, ——, Graham, O. H. & Ferguson, M. S., 435.
Baroody, B. J., 470.
Bates, M. & Roca-Garcia, M., 415.
Bedford, D. E., Aidaros, S. M. & Girgis, B., 433.
Bendich, A. & Chargaff, E., 407.
Benedek, T., with Lewe, I., Price, H., Koransky, A. & van Horn, F., 458.
Block, S. S., 467 *bis*.
Boiron, H., 429.
Brown, M. & Rennie, J. L., 395.
Burrows, W., Mather, A. N., Elliott, M. E. & Wagner, S. M., 422.
——, ——, McGann, V. G. & Wagner, S. M., 422.

Carruthers, L. B., 425.
Chu, L. W., & Huang, C. H., 423.
——, ——, Chang, C. T. & Kao, H. C., 423.
Clark, W. M., 400.
Cole, L. C. & Koepke, J. A., 468.
Cowper, S. G., 409.
Cristol, S. J., Haller, H. L. & Lindquist, A. W., 466.

Darby, W. J., Cherrington, M. E. & Ruffin, J. M., 456.
Dearborn, E. H., 403.
—— & Marshall, E. K., Jr., 403.
Dogiel, V. A., 477.
Doucet, G., 451.
Drew, R., Dixon, K. & Samuel, E., 453.

Einhorn, N. H. & Tomlinson, W. J., 393.
El Ayadi, M. S., 433.
Elmendorf, J. E., Jr., Marucci, P. E., Griffin, J. B., Meyer, S. L. & Ryan, G. S., 466.
Evans, E. A., Jr., 400.

Fairley, N. H., 398, 399.
Fajerstein, S. G. & Besdenjesznich, K. V., 409.
Federation Proc., 400.
Ferguson, M. S., Graham, O. H., Bang, F. B. & Hairston, N. G., 435.
Findlay, G. M., Hardwicke, J. & Phelps, A. J., 406.
Fletcher, O. K., Jr., 392.
Flinn, L. B., Howard, J. W., Todd, C. W. & Scott, E. G., 413.
Franks, M. B., 446.
Friess, 442.
Fulton, J. D. & Lourie, E. M., 403.

Gallenson, N., 413.
Gallut, J., 421.
Garcia Miranda, A., 431.
Gardner, A. D., 426.
Gersdorff, W. A. & Barthel, W. F., 467.
Gilliam, A. G., 408.
Gómez Marcano, A., 390.
Gordon, R. M. & Hill, M. A., 402.
Grasset, E., 419.

Haynes, D. M. & Hess, W. I., 460.
Hellerman, L., Bovarnick, M. R. & Porter, C. C., 400.
Hernández-Morales, F., Oliver-González, J., & Pratt, C. K., 434.
Hicks, J. D., 460.
Highby, P. R., 446.
Hollands, R. A. & Palmer, E. D., 439.
Huang, C. H. & Chu, L. W., 419.
Huebner, R. J., Jellison, W. L. & Pomerantz, C., 411.
——, Stamps, P. & Armstrong, C., 411.
Hunter, G. W., Ingalls, J. W. & Cohen, M. G., 440.

Ibarra Pérez, R. & González Prendes, M. A., 430.
Ignacio Chala H., J., 430.
Ingalls, J. W., Jr., 442.

Jadin, L. B. & Herman, F., 390.
Jaffé, R. & Ferro, R., 433.
Jersild, M. & Meulengracht, E., 457.
Johnstone, R. D. C., 396.
Jones, B., 469.
Jones, H. A., McCollough, G. T. & Morton, F. A., 467.

Kartman, L., 420.
Katzin, B. & Most, H., 440.
Kauntze, W. H., 470.
Knowles, F. L. & Smith, C. S., 399.
Kuntz, R. E. & Stirewalt, M. A., 434.

Laemmert, H. W., Jr., Ferreira, L. de C. & Taylor, R. M., 414.
van Laere, J., 394.
Landsborough, D. & Tunnell, N., 418.
Laurans, R., 468.
Levine, H. D. & Erlanger, H., 395.
Lewis, M. N., 406.
Lewthwaite, R., O'Connor, J. L. & Williams, S. E., 410.
Loeb, R. F., 396.
Lopez, G. G., Spies, T. D., Menendez, J. A. & Toca, R. L., 456.

Madden, A. H., Lindquist, A. W. & Knipling, E. F., 466.
Maegraith, B., 393.
Magrou, E., 417.
Malcomson, M. E. & Wishart, F. O., 407, 408.
Manson-Bahr, P. & Clarke, O., 456.
Matilla, V., Covaleda, J. & Aparicio Garrido, J., 443.
de Meillon, B., 469.
Meleney, H. E. & French, R. S., 410.
Milanes, F., Curbelo, A., Rodriguez, A., Kouri, P. & Spies, T. D., 452.
Molnar, G. W., Towbin, E. J., Gosselin, R. E., Brown, A. H. & Adolph, E. F., 461.
Most, H., Hayman, J. M., Jr. & Wilson, T. B., 443.
Murray, R. E., 476.

Continued overleaf.

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ALPHABETICAL LIST OF AUTHORS OR SOURCES—*cont. from page 3.*

Ober, R. E., 448.
Oppenheim, J. M., Whims, C. B. & Frisch, A. W., 449.

Packchanian, A. & Price, T. G., 429.
Page, F. T., 424.
Page, S. G., Jr. & McCall, J. V., Jr., 396.
Peltier, M., 417.
Perret-Gentil, A., 396.
Perry, W. J., 391.
Portwood, L. M. & Sanders, E., 448.

Reimann, H. A., Chang, G. C. T., Chu, L. W., Liu, P. Y. & Ou, Y., 428.
Ribbands, C. R., 463.
Robertson, K., 428.
Romaña, C. & Gil, J., 405.
——, —— & de Romaña, M. S., 404.
Roos, A., Hegsted, D. M. & Stare, F. J., 403.
Rosenthal, S. R. & Routien, J. B., 460.
Russell, H. K., Eisenhower, E. W. & Roose, D. J., 425.
Ryder, J. B. & Towson, R. T., 399.

Sabrosky, C. W., McDaniel, G. E. & Reider, R. F., 392.
Sapero, J. J., 472.
de Sarasin, G. S. W. & Pieris, M. V. P., 447.
Sashin, D., Brown, G. N., Laffer, N. C. & McDowell, H. C., with Boeing, P. J., 460.
Scott, J. A., 447.
Selby, C. H., 398.
Sharpe, D. S., 463.
Shute, P. G., 394.
Sicault, G., 426.
Sipton, J. A., 390.
Sokhey, S. S. & Wagle, P. M., 418.
Soliman, H. S. & Mohamed, A. H., 458.
Stoll, N. R., Loughlin, E. H., Harris, A. H. & Chenoweth, B. M., Jr., 444.
Stowman, K., 421.
Stunkard, H. W., 432.
Sullivan, R. R. & Ferguson, M. S., 435.
Sweigert, C. F., Turner, J. W. & Gillespie, J. B., 460.
Swellengrebel, N. H. & Schüffner, W. A. P., 448.

Taliaferro, W. H., 464.
Taylor, F. H., 476.
Taylor, R. M. & da Cunhá, J. F., 414.
Trembley, H. L., 402.

Van den Ende, M., Stuart-Harris, C. H., Fulton, F. & Niven, J. S. F., with others, 472.
Viswanathan, D. K., 391.

de Wardener, H. E. & Lennox, B., 450.
Wayson, N. E., McMahon, M. C. & Prince, F. M., 419.
Weinberg, H. B. & Tillinghast, A. J., 441.
Wendel, W. B., 400.
Willett, F. M. & Oppenheim, E., 460.
Wilson, D. J., 395.
Wittebolle, P. & Niemegeers, L., 427.
Wu, C. C., Ghosh, S. M., McClymont, A. G. & Roy, D. N., 464.

Yates, W. W., 466.